VOLUME 60 NUMBER 4

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VOLUME 60 APRIL 1950 NUMBER 4

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EFFECT OF TRANSPLANTATION OF BONE MARROW INTO IRRADIATED ANIMALS

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LOS ANGELES
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SINGLE dose roentgen irradiation to the whole body has been noted to produce conspicuous alteration in the hematopoietic system.[1] Chief of these alterations is the damage incurred to the bone marrow. The mechanism whereby this damage is incurred is the subject of a great deal of study, but it is well established that it results from the direct effects of irradiation.[2]

Since such damage to the hematopoietic tissues leads to severe disability and frequently to death, it becomes important to direct therapeutic measures that will offset or correct the derangements. The studies incorporated in this report were made primarily to determine what benefits, if any, may be derived from the transplantation of normal bone marrow in animals that have suffered damage to their bone marrow as the result of single dose roentgen irradiation.

Precise evidence for definite favorable results from transplantation of bone marrow is lacking. Neuhof [3] mentioned transplantation of bone

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This paper is based on work performed under contract no. W-7401-Eng.-49 for the Atomic Energy Project at the University of Rochester.

Determination of hemoglobin was carried out, but the results are not recorded here since the data provided little information.

1. Prosser, C. L.; Painter, E. E., and Swift, M. M.: The Clinical Physiology of Dogs Exposed to Single Total Body Doses of X-Rays, Metallurgical Laboratory, Chicago University, Report no. CH 3738. Shouse, S. S.; Warren, S. L., and Whipple, G. H.: Aplasia of Marrow and Fatal Intoxication in Dogs Produced by Roentgen Radiation of all Bones, J. Exper. Med. **58**:421 (March) 1931.

2. Lawrence, J. S.; Valentine, W. N., and Dowdy, A.: Is There an Indirect Effect of Radiation? Blood **3**:593, 1948.

3. Neuhof, H.: The Transplantation of Tissue, New York, D. Appleton & Company, 1923.

marrow along with transplantation of bone. The bone marrow in the graft degenerated in the first week, and connective tissue replaced it. Marrow reappeared after about five weeks but was probably derived from nearby marrow and not from a regeneration of that transplanted within the bone graft. Loeb [4] also briefly referred to the transplantation of bone marrow. Bone marrow transfusions have been used clinically in the treatment of various types of blood dyscrasias, but the results were inconclusive.[5] A suitable explanation for the successful transplantation of homologous corneal tissue in human beings is lacking.[6] Success has been claimed for cartilage [7] and bone homografts, although they are probably only of practical value in the support they offer during the healing process.

The work of Green [8] has demonstrated conclusively that homografts and heterografts of certain selected tissues have been placed on a successful basis. Successful transplantation to the anterior chamber of the eye of the guinea pig or rabbit has resulted with many heterologous embryonal tissues and with a wide variety of heterologous malignant tumors. Transplant failures have occurred with liver, benign tumors and potentially malignant tumors. Despite the success enjoyed in such a study, an explanation for the favorable results is wanting.

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4. Loeb, L.: Transplantation and Individuality, Physiol. Rev. **10**:547, 1930.

5. Osgood, E. E.; Riddle, M. C., and Mathews, T. J.: Aplastic Anemia Treated with Daily Transfusions and Intravenous Marrow: Case Report, Ann. Int. Med. **13**:357, 1939. Sanchez Yllades, L. S.: Ultimos estudios sobre la transfusión de médula, Medicina, México **23**:75, 1943. Sanchez Yllades, L. S., and del Castillo, H.: La medulotransfusion en las anemias secundarias: Notas preliminares, ibid. **22**:371, 1942; La transfusión de médula en algunos estados enfecciosos: Notas preliminares, ibid. **22**:624, 1942; La medulotransfusion en diversas hemopatias: Notas preliminares, ibid. **22**:283 and 268, 1942. Morrison, M., and Samwick, A. A.: Intramedullary Transfusion of Human Bone: Preliminary Report, J. A. M. A. **115**:1708 (Nov. 16) 1940.

6. Castroviejo, R., and Elliot, A. J.: Inclusion of Sclera in Corneal Transplantation; Gross and Microscopic Study, Arch. Ophth. **27**:899 (May) 1942.

7. Young, F.: Homogenous Cartilage Grafts: Experimental Study, Surgery **17**:616, 1945.

8. (*a*) Greene, H. S. N., and Lund, P. K.: Heterologous Transplantation of Human Cancers, Cancer Research **4**:352, 1944. (*b*) Greene, H. S. N.: Heterologous Transplantation of Embryonic Mammalian Tissues, ibid. **3**:809, 1943. (*c*) Greene, H. S. N., and Murphy, E. D.: Heterologous Transplantation of Mouse and Rat Tumors, ibid. **5**:269, 1945. (*d*) Greene, H. S. N.: Personal communication to the authors.

METHODS

The technics of hematologic study, irradiation and animal care have been described previously.[9]

SURGICAL TECHNIC

1. *Transplantation of Marrow Suspension.*—Marrow was removed from the shafts of femurs, humeri and occasionally tibias of anesthetized or recently killed normal donor dogs under strict aseptic procedures. The marrow was immediately suspended in an equal volume of a mixture of approximately one part of autologous serum and one part balanced salt solution[10] at 37 C. This suspension was then injected into the shafts of a right femur and in some instances into the shafts of the right humerus by means of a syringe with a 15 or 17 gage curved blunt needle. The needle was inserted through a snugly fitting drill hole in the distal part of the bone cortex, which was later plugged by means of bone wax on removal of the needle. Occasionally a second small drill hole was made at the proximal end of the long bone to relieve any pressure in the medullary cavity.

All recipient animals were anesthetized carefully with sodium pentothal by means of a constant intravenous drip.

Surgical wounds were handled with careful attention to hemostasis, strict asepsis and minimal trauma. Irradiated wounds were closed with absorbable sutures.

2. *Transplantation of Bone and Marrow.*—A rectangular bone cap devoid of periosteum, approximately 8 by 30 mm. in size, was excised from the midshaft of the femur of an anesthetized donor animal by means of a power saw. Care was taken to keep the endosteal lining and attached bone marrow intact. This bone cap with attached endosteum and marrow was then transplanted to the midshaft of the right femur of the recipient animal along with as much of the marrow as could be removed from the shaft. The recipient area was prepared by splitting the periosteum lengthwise, excising a bone cap by means of a power saw to match the donor bone cap and removing as much of the damaged bone marrow as necessary to receive the donor marrow. The donor bone cap was held in place by means of four fine absorbable sutures placed through minute drill holes located along the sides of the donor bone cap and the adjacent edges of the defect in the recipient femur. The periosteum was closed with multiple interrupted absorbable sutures.

3. *Transplantation of Rib.*—A section of the seventh, eighth or ninth rib on the right side, measuring 5 to 6 cm. in length, was removed without attached periosteum from the normal donor animal. The ends were pointed and minute holes drilled. A similar section of rib from the same region was removed from the recipient animal. The residual rib stumps were grooved and the donor specimen

9. (*a*) Rekers, P. E., and Coulter, M. P.: A Hematological and Histological Study of the Bone Marrow and Blood of the Adult Dog, Am. J. M. Sc., to be published. (*b*) Rekers, P. E.: Transplantation of Bone Marrow into Dogs that Have Received Total Body Single Dose Radiation, University of Rochester, Atomic Energy Project Report, UR-11. (*c*) Field, J. B., and Rekers, P. E.: Studies of the Effects of Flavonoids on Roentgen Irradiation Disease: I. Protective Influence of Rutin in Irradiated Dogs, Am. J. M. Sc. **218**:1, 1949.

10. Gey, G. O., and Gey, M. K.: The Maintenance of Human Normal Cells and Tumor Cells in Continuous Culture: I. Preliminary Report, Am. J. Cancer **27**:45, 1936.

fitted into position and held with fine absorbable sutures placed through the minute drill holes in the ends of the donor and recipient ribs. The periosteum was closed over the rib graft with multiple interrupted absorbable sutures and the wound closed in layers.

4. *Intravenous Transplantation of Marrow.*—Donor animals were prepared by massive bleeding of an estimated one half to one third of the total blood volume seven to nine times, beginning three weeks before donation. These bleeding procedures rendered the long bone marrow much more cellular and a great deal less fatty. At the time of donation the animals were killed by means of intravenous injections of air, the long bones removed asceptically and immediately split open and the marrow delivered into specially constructed, 50 cc. sterile centrifuge tubes containing 20 to 30 cc. of a mixture of approximately one part autologous serum and one part balanced salt solution.[10] Several sterile glass beads were placed in the tube, the tube stoppered and the contents shaken in a mechanical shaker for twenty to thirty minutes. After centrifuging for twenty minutes at 2,000 revolutions per minute, the floating particles and fat were suctioned off, the cells resuspended and the fluid removed for injection. The residue was treated by a second and third shaking and washing with similar fluid. All the fluid was pooled, warmed to 37 C. and injected slowly into the jugular vein by means of a syringe and needle. The tubes containing the marrow suspension were kept at 37 C. as much of the time as possible by means of a warm sodium chloride bath. Total and differential marrow cell counts were made on representative specimens of the suspension just before injection. Likewise, total nucleated, differential cell and platelet counts were made before and five minutes after transfusion.

5. *Transplantation to Anterior Chamber of Eye.*—The eye to be transplanted was anesthetized by the local application of a 5 per cent solution of cocaine when a general anesthesia was not used. The anterior chamber was opened at the superior margin of the corneoscleral junction by means of a small incision with a sharp corneal knife. A small amount of aqueous humor was allowed to escape and several fragments of bone marrow measuring approximately 1 mm. in diameter were inserted into the eye by means of a small syringe and a needle or trochar. The fragments were then forced into the inferior angle between the iris and the cornea by the application of light pressure along the corneal surface with a blunt instrument. The corneal incision closed spontaneously on removal of the instrument, so suturing was unnecessary. Corneal irrigations with isotonic sodium chloride solution were occasionally desirable for the first three to four days.

RESULTS OF TRANSPLANTATION OF BONE MARROW INTO DOGS GIVEN SINGLE DOSE IRRADIATION

Two groups of dogs were studied as controls for the following transplantation studies (table 1). The first group of 15 normal dogs received 350 r single dose irradiation of the whole body. Ten (67 per cent) of these dogs died of irradiation intoxication. A second group of 4 normal dogs in addition were subjected to pseudotransplantation of marrow two days after irradiation. Three (75 per cent) of these dogs died. In the dogs that died generalized purpura, panhematopenia, marked hypoplasia of the bone marrow, spleen and lymph nodes were the chief findings. This subject has been discussed in detail previously.[9b]

I. INTRAMEDULLARY TRANSPLANTATION

A. *Transplant of Marrow Suspension.*—A group of 5 normal dogs received 350 r single dose irradiation of the whole body and received a single normal transplantation of marrow suspension in the distal end of the shaft of the right femur, the right humerus and the anterior chamber of each eye.

Four of the 5 dogs died during the course of study (table 1). In those that died evidence of irradiation intoxication, similar to that noted in the control groups, was found. Primary healing of the operative wounds did not occur in 3 of the 5 dogs.

Hematologic Data: A comparison of the hematologic results in this group with the results in the corresponding control group shows no significant difference in the rate or degree of depression of the various peripheral blood elements following irradiation. The recovery phase, which is based on 1 dog only, shows no difference between erythrocyte values in this group and those in the corresponding control group. The platelet values show a suggestive increase over the control studies from the thirtieth to the sixtieth day after irradiation. A similar difference is noted in the reticulocyte values between the twentieth and fortieth days after irradiation. The total white blood cell count of the transplanted group is conspicuously increased over that of the control group from the nineteenth to the sixtieth day after irradiation. This difference can be attributed, for the most part, to the increase in the neutrophils. An increase in the lymphocyte values is present, however.

Pathologic Data: The bone marrow studies in this group, exclusive of transplanted sites, gave essentially the same results as those found in the control group.

The transplanted sites in the animals that died during the period of study showed some organizing blood clots, a marked inpouring of adult erythrocytes, nuclear debris, pyknosis and rarely a small islet of viable-appearing cells along the endosteal lining. Myeloid, erythroid and megakaryocytic cellularity was more conspicuous at the epiphysial ends. In the animal that survived for the sixty day period of study the non-transplanted marrow was conspicuously hyperplastic, with a pronounced increase in the myeloid, erythroid and giant cell components. There was little fat and no inpouring of adult erythrocytes, but numerous mitotic cells and an occasional clump of detritus were noted. This hyperplasia applied to long bones as well as flat bones. The marrow at the transplanted sites was similarly hyperplastic, but in addition there were small microscopic areas of organized blood clots and fibrosis.

Examination of marrow transplanted to the anterior chambers of the eyes revealed fat, degenerating cells, cellular debris and occasional microscopic old hemorrhagic areas in the animals that died, while in the

animal that survived true bone formation had occurred. Residual deposits of fat and some large blunt connective tissue cells were also present.

B. *Transplant of Bone and Marrow.*—A group consisting of 6 normal dogs received 350 r single dose irradiation of the whole body and received a transplant of normal bone marrow and accompanying bone cortex and endosteum to the shafts of the right femur and a transplant of a segment of rib to a rib two days after irradiation. A transplant of marrow suspension was placed in the anterior chamber of each eye at the same time.

Three of the dogs died during the course of study (table 1). In those that died irradiation intoxication was the outstanding feature. One animal suffered a fracture of the femur operated on. Primary

TABLE 1.—*Summary of Bone Marrow Transplantation into Dogs*

Group	Irradiation	Number of Dogs	Mortality, %
Control irradiated	350 r*	15	67
Control group which underwent irradiation and pseudo-marrow transplant	350 r*	4	75
Intramedullary			
Marrow suspension transplant I a	350 r*	4	80
Bone and marrow transplant I b	350 r*	6	50
Bone and marrow transplant III a (4)	2,000 r to both lower extremities	4	0
Extramedullary			
Intravenous marrow transplant II a	350 r*	14	43
Marrow transplant to spleen II b (1)	none	4	0
Marrow transplant to spleen II b (2)	2,500 r to spleen	4	0
Marrow transplant to spleen II b (3)	350 r*	4	75

* Single dose irradiation of whole body.

healing of the operative wounds did not occur in 4 of the 6 dogs. Two of the four separated wounds healed after irrigation and resuturing.

Hematologic Data: A comparison of the hematologic results in this group with the results in the corresponding control group and the group which received a transplant of marrow suspension shows no significant difference in the rate or degree of depression of the various peripheral blood elements following irradiation. The recovery phase is essentially the same as that noted in the group which received a transplant of marrow suspension.

Pathologic Data: The bone marrow studies in this group, exclusive of the transplanted sites, gave essentially the same results as those found in the control irradiated group.

The transplanted sites of the femurs of those animals that died were similar to those in the group that received a transplant of marrow suspension with the exception that there was more evidence of organized blood clots, debris and abundant new bone formation in the intramedullary and subperiosteal areas. The transplanted ribs of these dogs

were solid, with evidence of new bone formation at each end. The marrow cavities were completely aplastic and filled with detritus. One dog was intentionally killed twenty-three days after irradiation and showed a hypoplastic marrow throughout, with only an occasional islet of viable-looking cells. The transplanted site of the femur was acellular except for an occasional islet of viable-looking cells and organized blood clots. The marrow of the transplanted rib was completely dead. The anterior

Fig. 1.—Cross section of femur sixty days after irradiation. Normal homologous bone and marrow transplant two days after irradiation to femur of dog that received 350 r to the whole body. Bone graft fixed in place by dense fibrous growth with marked intramedullary and subperiosteal bone growth. Hyperplastic marrow attached to recipient endosteum opposite graft site. × 13.

chamber transplants showed residual fat deposits with nuclear debris and occasionally small hemorrhagic areas.

The remaining 2 dogs that survived and were examined sixty-three and sixty-four days after irradiation showed a hyperplastic marrow

similar to that noted in the surviving animals in the control group with the exception that in the transplanted femur there were more organized blood and intramedullary and subperiosteal bone growth (fig. 1).

A review of the bone and marrow transplants to the medullary regions in this laboratory indicates that evidence of degeneration of the bone and the bone marrow appears in a few days. Coincident with the absorption of the bone, the process of substitution of the dead bone by new osteoid tissue goes on. About the eighth day the transplant becomes permeated by a richly vascular connective tissue, and in some places these are islands of new bone. The cells of the bone marrow lose their nuclei, many are filled with fat deposits and between the cells are found many polymorphonuclear leukocytes if the recipient has not received irradiation. The blood vessels in the marrow spaces degenerate and become filled with fibrin, but a few contain some red blood cells. A connective tissue replacement of the marrow then begins. In less than four weeks a graft of the diaphysis shows massive fibrous tissue replacement of the marrow; this process is not so extensive in an epiphysial graft examined after the same period. The connective tissue replacing the marrow is rich in vessels. After a month the vascularity becomes progressively less marked and the tissue becomes less cellular. Regeneration of the myeloid cell elements is seen in the perivascular spaces, and at the end of about five weeks there is a richly developed myeloid tissue grouped characteristically around fat cells. The regeneration process of the marrow is of hematopoietic origin, but whether these new cells are derived from the endothelium or the adventitia of blood vessels or from the reticulum has not been determined. In view of the histologic changes in the bone marrow, it is fair to assume that death and replacement occur rather than regeneration from persisting portions of the transplanted marrow.

II. EXTRAMEDULLARY TRANSPLANTATION

A. *Intravenous Transplantation of Marrow.*—Previous experiments have indicated that bone marrow could not be transplanted successfully into intramedullary sites. Furthermore, such transplant procedures entailed formidable surgical procedures which in themselves were injurious to the irradiated host and permitted the transplantation of small quantities of marrow only. In view of these observations the intravenous route was selected as a possible pathway for the administration of bone marrow.

Fourteen normal dogs that received single dose irradiation of the whole body with 350 r followed by intravenous transplantation of marrow two, four, seven and nine days after irradiation were studied. Six of the 14 (43 per cent) dogs died of intoxication between thirteen and eighteen days after irradiation (table 1). Postmortem findings con-

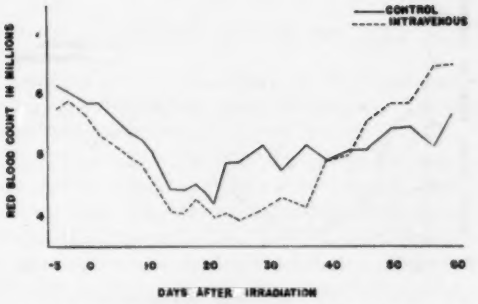

Fig. 2.—Mean values for red blood cell count after intravenous injection of marrow following irradiation to the whole body.

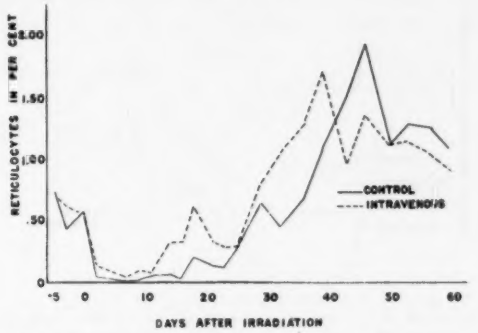

Fig. 3.—Mean values for reticulocyte count after intravenous injection of marrow following irradiation.

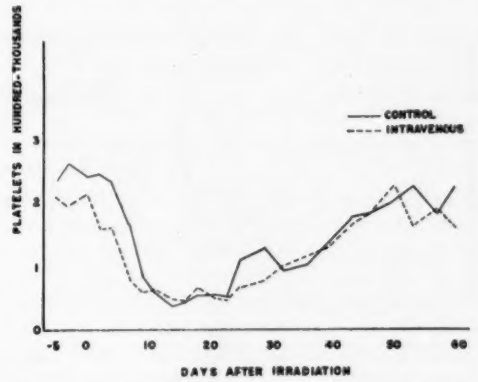

Fig. 4.—Mean values for platelet count after intravenous injection of marrow irradiation.

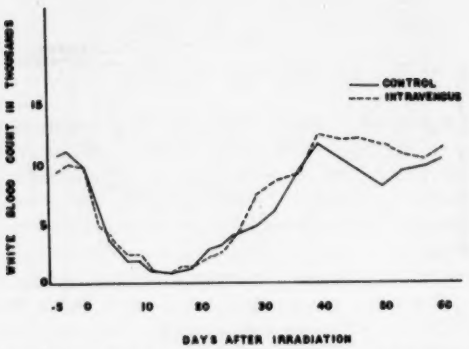

Fig. 5.—Mean values for white blood cell count after intravenous injection of marrow following irradiation.

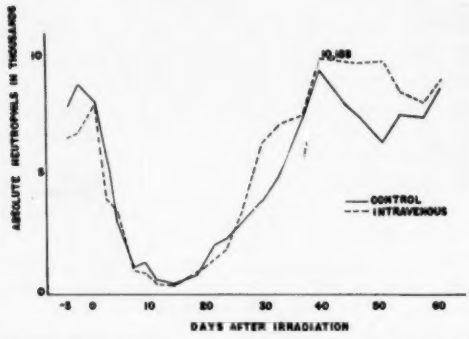

Fig. 6.—Mean values for absolute neutrophils after intravenous injection of marrow following irradiation.

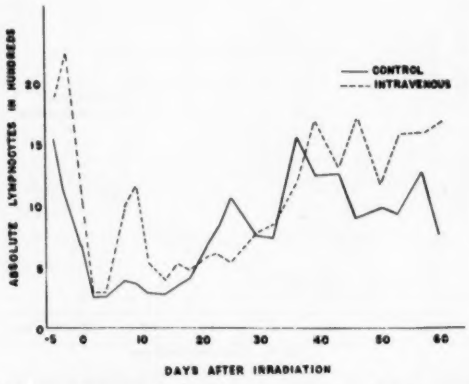

Fig. 7.—Mean values for absolute lymphocytes after intravenous injection of marrow following irradiation.

sisted of generalized purpura, hypoplasia of the hematopoietic system, panhematopenia and occasionally generalized sepsis. The purpura and sepsis were not as marked as in the control group.

Hematologic Data (figs. 2 to 8): The peripheral blood picture of these animals differed from that of the control group in that the depression of the white blood cells was not as uniform or as great (table 2). Transient increases of the total white blood cell count were encountered, and during these increases several types of atypical or unclassified cells were found. One of these types of cells resembled a blast form, and another type was vaguely similar to a monocyte but not identifiable as such with the supravital technic.

The absolute lymphocyte values for the group given a transplant of marrow showed an increase over the control group from the seventh

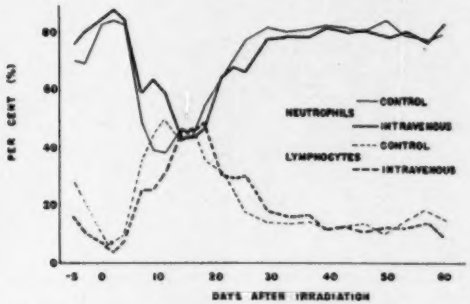

Fig. 8.—Mean values for differential count after intravenous injection of marrow following irradiation.

to the eighteenth day after irradiation, with a peak occurring about the ninth day, when the last transplantation had occurred (table 3).

In summary, it appears that the total white blood cell count, the absolute lymphocyte value and the reticulocyte value of the peripheral blood are increased slightly after the transfusion of bone marrow intravenously (tables 2, 3 and 4).

Pathologic Data: Pathologic study of the 6 animals dying of irradiation intoxication showed the same changes as those noted in the animals dying in the control irradiated group. The lungs presented many small calcific deposits within the lumen of small veins (fig. 9). In most instances these deposits were firmly attached to the vessel wall and frequently showed a surrounding rim of cells suggesting osteoblasts. There were occasionally a few cells suggesting lymphocytes surrounding such vessels but no other cellular reaction. Some of the alveoli were filled with fluid and a few with blood, while a few of the alveolar walls showed

evidence of disintegration. A cellular exudate in the bronchi or alveoli was not found.

The pathologic study of the 8 animals surviving for the entire period of study showed a hyperplastic marrow, moderate hyperplasia of the

TABLE 2.—*Comparative Leukocyte Values*

Days After Irradiation	Total White Blood Cell Count		
	Control	Transplanted	Difference
4	3,600	4,200	+0,600
5	3,200	3,400	+0,200
7	1,800	2,460	+0,660
9	1,900	2,500	+0,600
11	1,050	1,100	+0,050
14	0,700	0,800	+0,100
16	0,800	1,200	+0,400
18	1,200	1,500	+0,300
21	1,900	2,200	+0,300
23	2,700	2,600	−0,100

TABLE 3.—*Comparative Lymphocyte Values*

Days After Irradiation	Absolute Lymphocyte Count		
	Control	Transplanted	Difference
2	250	300	+ 50
4	260	300	+ 40
5	330	330	...
7	390	1,080	+690
9	370	1,190	+820
11	310	560	+250
14	293	414	+121
16	315	550	+135
18	415	500	+ 85
21	700	600	−100

TABLE 4.—*Comparative Reticulocyte Values*

Days After Irradiation	Reticulocyte Values, %		
	Control	Transplanted	Difference
2	0.04	0.15	+0.11
4	0.03	0.10	+0.07
5	0.04	0.18	+0.14
7	0.00	0.05	+0.05
9	0.03	0.10	+0.07
11	0.05	0.08	+0.03
14	0.06	0.31	+0.25
16	0.03	0.33	+0.30
18	0.20	0.61	+0.41
21	0.14	0.34	+0.20
23	0.13	0.29	+0.16
25	0.28	0.30	+0.02
29	0.64	0.80	+0.16
32	0.44	1.04	+0.60
36	0.68	1.28	+0.60

spleen and lymph nodes and spotty hypertrophy of the mucosa of the gastrointestinal tract. The lungs were studded with many small areas of bone formation surrounded by a rim of osteoblast-like cells, all within small veins (fig. 10). The bone was intimately attached to the vessel wall, and a small lumen or recanalization was noted in many instances.

Grossly, such calcified areas occasionally measured 7 to 8 mm. in diameter, but usually these areas were miliary in size and more easily detected on the pleural surfaces of the lungs.

The transplantation of bone marrow intravenously was associated with a decrease in the mortality and morbidity as well as a slightly less pronounced depression of the total white blood cell, absolute lymphocyte and reticulocyte values than that in a control group of dogs. The lungs

Fig. 9.—Lung twenty days after irradiation to the whole body (350 r) and eighteen days after intravenous injection of marrow. Bone spicules with only a few osteoblast-like cells and round cells within pulmonary vein. Pulmonary congestion and edema. × 100.

of the animals given a transplant were studded with multiple bone spicules within the pulmonary veins which were surrounded by a rim of cells.. Typical myelopoiesis at these sites could not be identified.

B. *Transplantation of Marrow to Spleens.*—The spleen was also selected as a possible pathway for administratior of bone marrow

because this has been reported to be a hematopoietic organ of some importance in the embryo.[11]

(1) Transplantation to Normal Spleens: Four normal dogs received transplants of normal bone marrow suspension to the right side of the spleen. None of the animals died or manifested complications as the result of the transplantation procedure (table 1). No significant alteration was noted in the hematologic picture. Pathologic study revealed

Fig. 10.—Lung sixty days after irradiation to the whole body, 350 r, and intravenous marrow transplantation. Transplant tissue in pulmonary vein shows bone spicules, dense fibrous connective tissue, recanalization and subintimal cellular proliferation. × 100.

residual fat deposits, pigmentation, a few lymphocytes, phagocytes and connective tissue cells but no definite evidence of extramedullary myelopoiesis at the site of transplantation.

11. Theil, G. A., and Downey, H.: The Development of the Mammalian Spleen with Special Reference to Its Hematopoietic Activity, Am. J. Anat. **28**:279, 1921.

(2) Transplantation to Heavily Irradiated Spleens: Four normal dogs received 2,500 r single dose irradiation to the splenic region and transplants of normal bone marrow suspension to the right side of the spleen two days after irradiation (table 1). One of the dogs manifested dehiscence and infection of the abdominal wound. All of them showed a decreased dietary intake, diarrhea and hemafecia for a brief period, seven to ten days after irradiation.

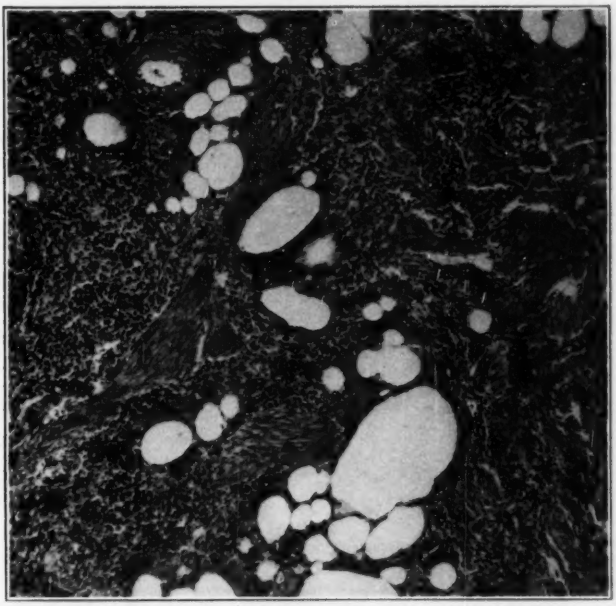

Fig. 11.—Normal bone marrow transplantation to spleen after irradiation to whole body. Hypoplastic spleen with residual fat deposits. × 100.

Hematologic studies showed no significant depression of any of the peripheral blood elements. There was a slight and transient decrease in the absolute lymphocytes immediately after irradiation. Pathologic study showed a relatively small hypoplastic and fibrotic spleen in which there were residual deposits of fat, pigmentation and increased connective tissue formation but no definite evidence of extramedullary myelopoiesis at the site of transplantation.

(3) Transplantation to Spleens of Dogs Given Irradiation to the Whole Body: A group of 4 normal dogs received single dose irradiation

to the whole body and transplants of normal bone marrow suspension into the spleen two days later. Three of the 4 dogs died of irradiation intoxication with generalized purpura, hypoplasia of the hematopoietic system, panhematopenia and generalized sepsis (table 1).

The peripheral blood picture was similar to that of the control group which underwent irradiation without transplantation (figs. 18 to 21). Pathologic study of the 3 animals dying of irradiation intoxication showed the usual changes noted in the control irradiated group. The spleens

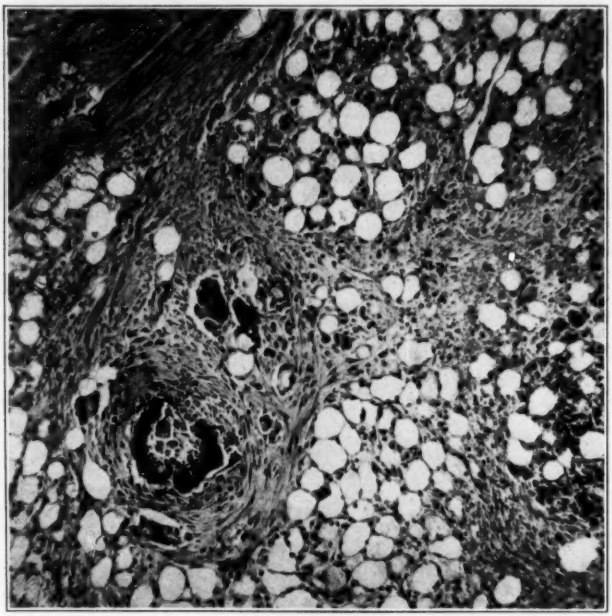

Fig. 12.—Microscopic appearance twenty-one days after homologous marrow transplant to subcutaneous region of ear of rabbit. Further loss of marrow cells with phagocytosis and residual syncytia, fat and early bone formation. × 100.

were hypoplastic and hemorrhagic, with residual deposits of fat and pigmentation at the sites of transplantation but without evidence of extramedullary myelopoiesis (fig. 11). The animal that survived for the designated period of study, sixty days, showed slightly hyperplastic marrow, hyperplastic malpighian corpuscles of the spleen and hyperplastic germinal centers of the lymph nodes. The usual residual fat and pigment deposits with scant round cell infiltration but without extramedullary myelopoiesis were noted at the sites of transplantation.

In summary, it is apparent that the transplantation of homologous normal adult marrow to the spleen has been without success irrespective of whether the spleen has been normal or irradiated.

C. *Transplantation of Marrow to Eye, Subcutaneous Tissue, Muscle and Peritoneum.*—Normal homologous femoral marrow from adult rabbits was transplanted to the anterior chamber of the eye, the sub-

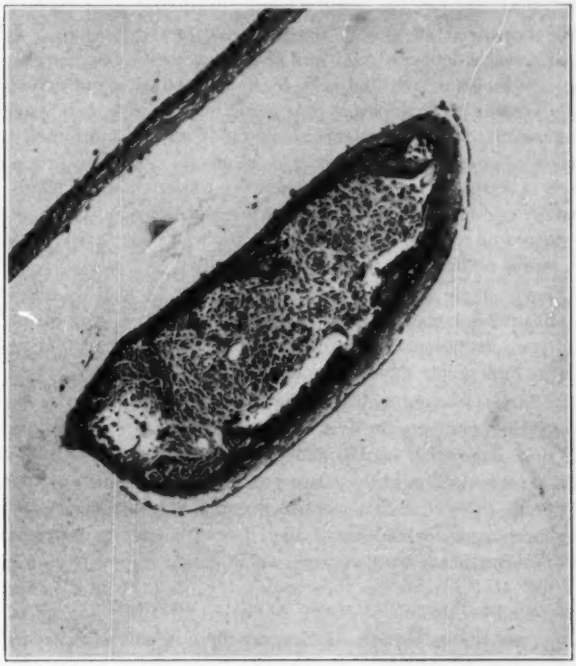

Fig. 13.—Microscopic appearance twenty-one days after homologous marrow transplant to anterior chamber of eye of rabbit. Conspicuous bone formation with lacunas. × 100.

cutaneous region of the dorsum of each ear and the muscular and peritoneal surface of the abdomen.

After transplantation, the eye implants were first reddish pink for three to five days and then became yellow or white with marginal vascularity if attached to the iris or gray if free and floating in the anterior chamber. Frequently the cornea became steamed and obscured visualization of the underlying structure. Attachment to the lens and cornea

occurred occasionally. Mild conjunctivitis frequently appeared early and subsided in most instances. Occasionally a residual persistent rim of erythema and increased vascularity was noted at the corneoscleral junction. At no time did the implant proliferate to fill the anterior chamber and cause the cornea to bulge. The ear implants initially were soft, large and rounded. Gradually they decreased in size and became more firm and within two weeks had a cordlike consistency. Occasionally an abdominal implant was palpable.

The transplant sites, with the exception of the peritoneal surface, showed residual deposits of fat in a syncytium with a few marrow cells. Phagocytosis, giant cells and cells laden with blood pigment were frequently present. The apparent phagocytic reaction was more marked in the transplants to the subcutaneous region of the ear and muscle of the abdomen. Bone formation, which was frequently noted, was occasionally present as early as the seventh day after transplantation. This bone formation was microscopic in size and usually surrounded by a rim of cells suggesting osteoblasts. Rarely was any tissue suggestive of marrow found on the peritoneal surface (figs. 12 and 13).

Although these studies were carried out for as long as twenty-one days after transplantation, there was no evidence to indicate that a successful transplantation of bone marrow had taken place or that marrow cells were undergoing multiplication or maturation.

D. *Transplantation of Marrow to Liver.*—Normal homologous marrow was transplanted to the liver of 4 dogs and 5 rats which had received single dose irradiation of 350 and 650 r respectively. The course of irradiation intoxication in these two groups of animals did not appear to be different from that in a control group, while the transplant sites showed a phagocytic and connective tissue reparative process rather than a proliferation of bone marrow.

III. EXPERIMENTS TO EXPLAIN THE RESULTS

From the studies carried out thus far there is little evidence to indicate that marrow could be transplanted successfully to normal marrow-bearing areas or that extramedullary myelopoiesis could be induced in the sites so tested. The exception to this finding, possibly, is the intravenous transplantation of marrow. In an effort to determine the cause of this failure, the following factors known to influence tissue transplantation were investigated: demand on the part of the recipient, quantity of material transplanted, adequate vascularization of the transplant, compatibility of donor and recipient marrow and age and development of the transplanted material.

A. *Stimulus for Bone Marrow Growth.*—Since there may have been an insufficient demand on the part of the recipient to encourage the

transplanted bone marrow to grow, stimuli for bone marrow growth were established before transplantation as follows:

(1) One group of rabbits was rendered markedly anemic by means of acute bleeding over a period of three weeks, with the reduction of the red blood count from 5,600,000 to 2,900,000 and of the hemoglobin content from 11.9 to 6.7 Gm. per hundred cubic centimeters.

(2) A second group of rabbits received subcutaneously 3 doses of 0.04 Gm. of phenylhydrazine over a period of three days, as a result of which the red blood cell count dropped from 5,900,000 to 2,000,000 and the hemoglobin content from 12.7 to 4.9 Gm., without any consistent alteration of the white blood cell count.

(3) A third group of rabbits received single dose irradiation of 350 r.

Bone marrow transplants to these irradiated or stimulated animals produced essentially the same clinical and pathologic picture as that noted in the normal or nonirradiated group.

(4) Four normal dogs received 2,000 r to each entire lower extremity followed by transplantation of marrow to the right femur only two days later. Two of these dogs received transplants of marrow suspension, and the other 2 received bone and marrow transplants into the right femurs.

None of the dogs died during the period of study, and only mild disturbances in weight and appetite were noted (table 1). All dogs showed the usual changes in the irradiated skin, namely, edema, erythema and loss of nails and desquamation of the foot pads. All wounds healed by first intention.

Only mild depression of the peripheral blood elements was noted after irradiation and operation.

Histologic examination of the transplanted femurs showed debris, hemorrhage and organization of blood and only scant evidence of marrow cellularity (figs. 14 and 15). Most of the cellularity was located on the perimeter of the marrow cavity adjacent to the endosteal lining. In the 2 dogs in which bone was transplanted along with the marrow, there was firm union between the donor bone and the recipient bone (fig. 16). The nontransplanted femur was only slightly more cellular than the transplanted side but lacked hemorrhage and organization. Here, too, the residual marrow cells were located on the perimeter of the marrow cavity. The nonirradiated bone marrow appeared to be normal.

From these results it is apparent that 2,000 r single dose irradiation to the lower extremity of a dog is insufficient to destroy all the bone marrow parenchyma. However, there is little evidence of regeneration thirty or fifty days after irradiation. Furthermore, homologous marrow, either as a marrow suspension or with bone, transplanted to irradiated

extremities does not appear to promote the regeneration of new marrow. The finding that destruction of bone marrow occurred only in the irradiated fields may be regarded as further evidence supporting the belief that the effect of irradiation on the hematopoietic system is a direct one.

Fig. 14.—Femur and diaphysis sixty days after transplantation. Irradiation to both lower extremities, 2,000 r. Marrow suspension transplant to this region of the femur. Dead marrow with organized blood clot, residual syncytia and fat. × 100.

From these observations it was concluded that the lack of stimulation for bone marrow growth, as herein applied, is an insufficient explanation for the failure of growth of homologous marrow.

B. *Sufficient Quantities of Marrow.*—Although a satisfactory answer cannot be supplied at this time, some points of interest can be presented. If one inquires as to the space occupied by bone marrow, values in the

range of 300 cc. for a medium-sized dog are found. However, a good deal of this space, especially in the long bones, is occupied by fat. Expressed differently, the amount of marrow necessary to reduce severe irradiation intoxication is probably that amount contained in one entire

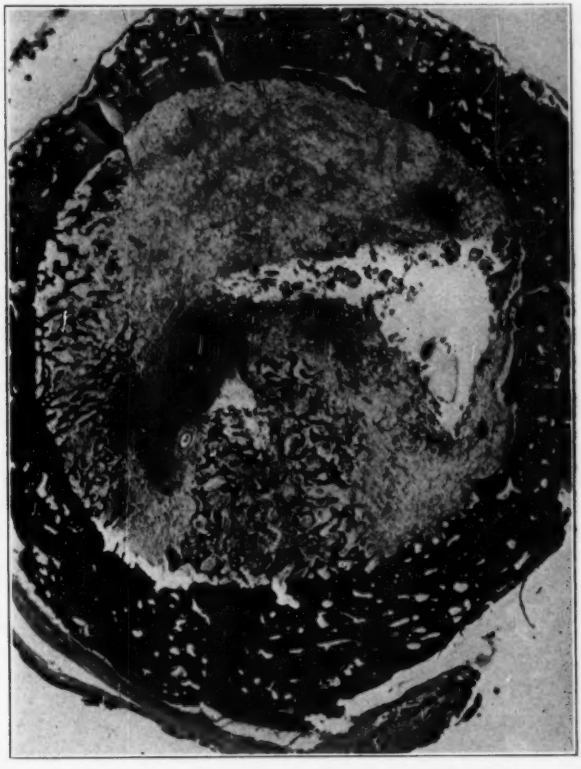

Fig. 15.—Cross section of femur sixty days after normal homologous marrow suspension transplant two days after irradiation of femur of dog that received 2,000 r to both lower extremities. Intramedullary bone growth, organized blood clot and no active marrow. × 13.

extremity or approximately two vertebrae.[12] Studies in this laboratory with shielding experiments have shown that the amount of marrow in

12. Warren, S. L., and Whipple, G. H.: Roentgen Ray Intoxication: II. A Study of the Sequence of Clinical, Anatomical and Histological Changes Following a Unit Dose of X-Rays, J. Exper. Med. **35**:203, 1922.

one entire lower extremity is hardly sufficient for protection from irradiation.[9b] With this information, then, the experiments herein reported were deficient in the quantity of marrow transplanted. The possible exception to this was the intravenous transplant group in which there was a suggestive benefit from the procedure. Here the recipient animal received the equivalent amount of marrow from all the long bones of a

Fig. 16.—Cross section of femur sixty days after irradiation. Normal homologous bone and marrow transplant two days after irradiation to femur of dog that received 2,000 r to both lower extremities. Conspicuous intramedullary and some subperiosteal bone growth. No active marrow. × 13.

donor animal on four different occasions, or, expressed in another way, each of the recipient animals received approximately 20×10^9 nucleated marrow cells with each transfusion of marrow. This quantity of cells injected into a dog with a blood volume of 1,000 cc. theoretically should elicit a rise in the nucleated cell count if the cells were maintained in

circulation. Table 5 indicates that a conspicuous rise in the total nucleated cell count was not found. Studies concerning the fate of these injected cells will be the subject of a subsequent report.

C. *Adequate Vascularity.*—One of the fundamental principles for the successful transplantation of any tissue is a provision for an adequate blood supply. When bone marrow is transplanted to its normal sites, such as the shaft of long bones, bleeding to the extent of frank hemorrhage is induced within the marrow cavity. This bleeding occurs after the simplest type of manipulation, even when the finest dental drill is passed through the bone cortex. Furthermore, it is accentuated after irradiation. However, this type of blood supply cannot be regarded as of much benefit to the transplanted cells since it initially causes a tamponade effect and then undergoes organization and a reparative process.

TABLE 5.—*Total Nucleated Cell Count Following Intravenous Transplantation of Marrow*

	1st Transfusion			2nd Transfusion			3rd Transfusion			4th Transfusion		
		Cells/Mm.³			Cells/Mm.³			Cells/Mm.³			Cells/Mm.³	
Dog No.	No. of Cells Injected	Before	After	No. of Cells Injected	Before	After	No. of Cells Injected	Before	After	No. of Cells Injected	Before	After
5	11.4×10^9	3,200	3,800	.....	.....	.....	37.7×10^9	2,600	10,250	30.9×10^9	5,150	9,600
6	11.4×10^9	5,300	8,900	.....	.....	.....	22.8×10^9	2,300	3,200	30.9×10^9	1,900	6,250
7	30.9×10^9	7,100	4,050	31.5×10^9	1,000	9,100	13.7×10^9	800	3,500	.....	.....	.....
8	30.9×10^9	6,100	9,100	156.2×10^9	3,550	3,950	31.5×10^9	1,700	6,250	13.7×10^9	1,250	4,000
9	12.2×10^9	4,750	5,100	18.9×10^9	5,400	8,700	6.2×10^9	2,950	2,450	32.4×10^9	2,800	4,450
10	.....	.....	.....	18.9×10^9	2,550	3,350	6.2×10^9	855	1,150	12.5×10^9	2,300	5,200
11	26.8×10^9	3,100	5,200	22.1×10^9	4,550	5,200	21.8×10^9	1,111	3,350	15.9×10^9	3,500	2,000
12	15.1×10^9	5,750	5,350	22.1×10^9	2,250	5,550	21.8×10^9	5,100	6,900	15.9×10^9	1,800	5,650
13	13.3×10^9	1,950	1,650	.....	.....	.....	.....	.....	.....	.....	.....	.....
14	13.2×10^9	600	3,050	.....	.....	.....	.....	.....	.....	.....	.....	.....
Mean	18.3×10^9	4,206	5,133	45.0×10^9	3,217	5,142	20.2×10^9	2,177	4,631	21.7×10^9	2,671	5,396
Mean increase		927			1,925			2,454			2,722	

No change in count after injection..... 76.7%
Increase in count after injection..... 16.7%
Decrease in count after injection..... 06.7%

When a rib is transplanted to a rib and its periosteal bed, the lack of vascularity is marked. The transplanted rib and the contained marrow die, and marginal vascularity is supplied slowly from the periosteum and the cut ends of the recipient rib, while the transplanted bone forms a framework which is absorbed and replaced by new bone formation.

Because of the finding of a poor blood supply for the transplanted tissue, the bone marrow was placed directly into the circulating blood, since it was anticipated that it would be deposited along vascular pathways and thus be provided with an adequate blood supply. Such a procedure resulted in either the deposition of or, probably more likely, the formation of multiple bone spicules within the pulmonary veins. Such bone was noted as soon as fourteen to fifteen days after irradiation or five to twelve days after transplantation and was invariably associated with a surrounding rim of cells suggesting osteoblasts but never

with any cells suggesting a nidus of bone marrow parenchyma. Other groups of animals received marrow transplants in multiple small deposits into the spleen and liver. It was felt that with such a procedure the transplanted marrow would have a reasonably good chance of having an adequate blood supply because of the normal abundant sinusoids. However, this transplanted marrow was readily phagocytized, with residual deposits of fat only being demonstrated.

From these experiments it seemed evident that though an adequate vascularity had been supplied to the donor material in some instances this factor alone was insufficient to explain the failure of the graft to take.

D. *Compatibility of Donor and Recipient.*—If the failure of the transplants to grow is because of incompatibility, then it becomes desirable to ascertain whether or not sensitivity or incompatibility can be altered. Is it a fact, as claimed, that cells grown in tissue culture lose their individuality and can be successfully and permanently transplanted, as, for example, the cells of the parathyroid glands? Higgins and Ingle [13] state that the adrenal cortex of newborn rats may be permanently homotransplanted into adults and gives evidence of functioning. Bloom [14] has grown autologous embryonal bone marrow successfully in the anterior chamber of guinea pigs after it had passed through tissue culture. Can the individuality of a cell be altered to permit successful transplantation as the result either of irradiation of the donor or irradiation of the recipient? In order to provide answers in part to these questions, marrow from the long bones of 4 normal adult checker rabbits, 4 normal adult dogs and 4 adult dogs that had recovered from single dose irradiation of the whole body administered sixty days previously was cultivated separately in a heterologous medium consisting of chicken plasma, beef embryo juice, newborn beef serum and a balanced salt solution for twenty-four to forty-eight hours and then transplanted to the anterior chamber of the eyes of normal homologous recipients. In no instance did the transplant proliferate to fill the anterior chamber of the eye, while gross and pathologic examination showed no significant difference in the transplants made directly to the eyes and those passed through tissue culture mediums. It must be recognized that the number of experiments conducted was few, however.

Another group of 4 dogs that had received irradiation of 350 r were given intravenous transplants of the hyperplastic marrow from dogs that had been exposed to and recovered from irradiation of 350 r sixty days previously. All the 4 recipient animals died of irradiation intoxication

13. Higgins, G. M., and Ingle, D. J.: Functional Homioplastic Adrenal Grafts in the Rat, Proc. Staff Meet., Mayo Clin. **12**:69, 1937.

14. Maksimov, A., and Bloom, W.: Textbook of Histology, ed. 2, Philadelphia, W. B. Saunders Company, 1934, p. 136.

in less than twenty days after irradiation, with hematologic and pathologic findings as noted in the control irradiated group.

In addition, conventional agglutination studies of the donor bone marrow cells and the recipient serum and vice versa failed to show evidence of incompatibility.[14a]

These experiments seemed to provide sufficient evidence that the donor cell could not be rendered more susceptible to transplantation by

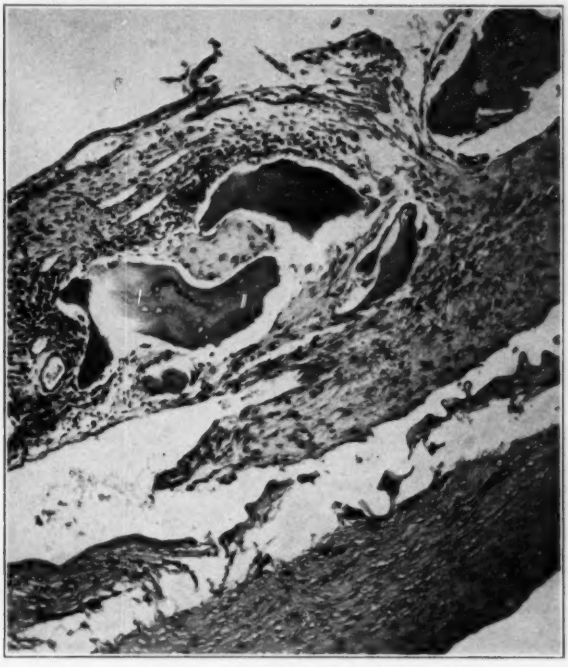

Fig. 17.—Microscopic appearance of eye one hundred and sixty-four days after homologous marrow transplant to anterior chamber of eye of rabbit. Loss of marrow cells with fibrous tissue and bone formation; vascular channels within graft. × 100.

passing the transplant material through tissue culture mediums or irradiation of either donor, recipient or both.

E. *Homogeneity Versus Autogeneity.*—In the light of the information given, the next factor logically to be studied was whether or not

14a. Since this report was submitted, the studies of Young and others (Science **109**:630, 1949) have clarified further hemagglutinins of dogs.

the failure of the marrow grafts to grow successfully was a function of homogeneity. Accordingly, bone marrow from the rabbit's own femur (autologous graft) was transplanted immediately to the anterior chamber of the eyes, the subcutaneous region of the dorsum of the ears and the muscle of the anterior abdominal wall. These grafts remained in the animal for as long as six months and were compared with homologous grafts of approximately the same duration. The autologous transplants

Figure 18.—One hundred and seventy-six days after autologous marrow transplant to anterior chamber of eye of rabbit. Loss of marrow cells with residual syncytia, fat, fibrosis and extensive bone formation. Note vascular channels within graft. × 100.

to the eyes remained pinkish red for a period of three to fourteen days and then gradually showed evidence of vascularity of the perimeter. Corneal steaming was frequently noted but was not as intense as that noted in the homologous transplants. Bone spicules with surrounding osteoblasts were common. Occasionally a small clump of normal-appearing marrow cells was found in which erythroid and myeloid ele-

ments could be identified. Phagocytosis, pigment deposition and connective tissue and bone formation were common findings. They forced one to conclude that adult autologous or homologous marrow transplanted to the anterior chamber of an eye underwent essentially the same fate, that of phagocytosis, connective tissue and bone formation (figs. 17 and 18).

F. *Age and Development of Donor Marrow.*—The work of Greene strongly suggests that many types of embryonal tissue, with the exception of liver and certain portions of the nervous system, can be trans-

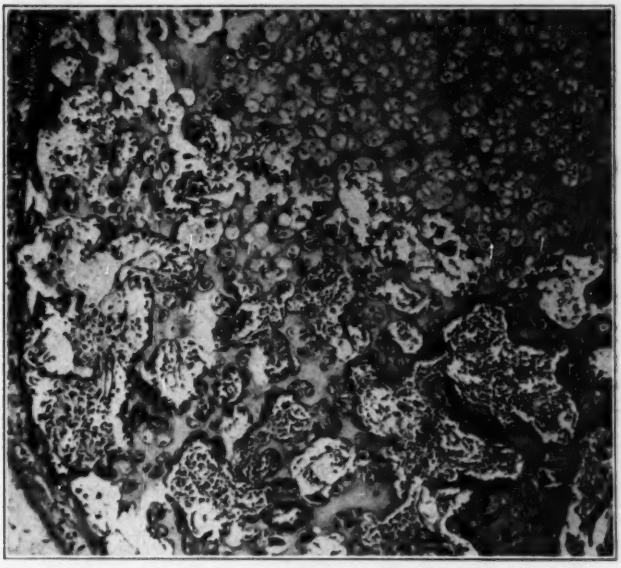

Fig. 19.—Fifty days after autologous embryonic limb bud transplantation to anterior chamber of eye of rabbit. Cartilage, epiphysis, bone and possibly early marrow formation. × 100.

planted successfully to the anterior chamber of the eye and in some instances to other regions of alien hosts. In this work, however, there are few data to indicate the results of transplantation of portions of the hematopoietic system, the bone marrow in particular. The explanation for the favorable results following transplantation of embryonal tissue is postulated to be that cells of the embryo are in an intermitotic stage.[8d]

Accordingly, autologous, homologous and heterologous embryonic bone marrow and mixed embryonic tissue containing hematopoietic

tissues were transplanted immediately to irradiated and normal hosts. Since the separation of bone marrow from small embryonic long bones was difficult, the entire embryo was minced into small pieces and these pieces distributed over a relatively large area so that adequate vascularity was supplied.

Transplantation to Normal Hosts: (A) Human limb buds from a 2 month old embryo were transplanted to the anterior chamber of the eyes

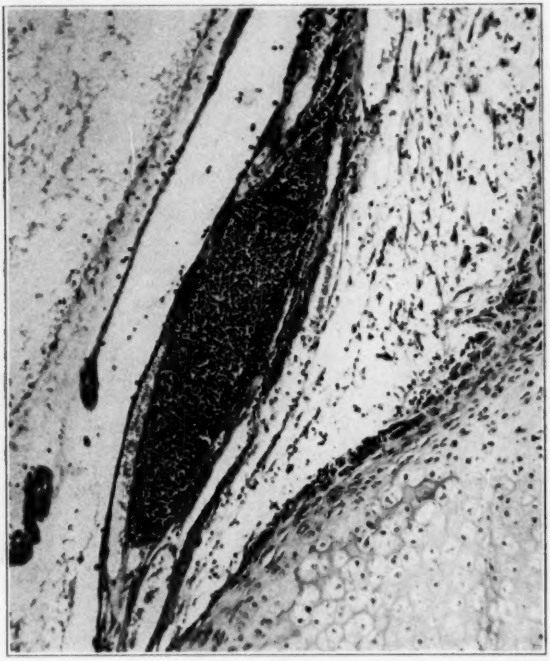

Fig. 20.—Forty-three days after autologous mixed embryonic transplant to anterior chamber of eye of rabbit. Developing cartilage and lymph follicle. × 100.

of guinea pigs. (B) Autologous and homologous dog embryonic spleen, bone marrow and entire minced embryos were each transplanted to the anterior chamber of the eyes and the anterior abdominal wall of dogs. (C) Spleen and bone marrow of beef embryos were transplanted to the anterior chamber of the eyes of guinea pigs, rabbits and dogs and to the anterior abdominal wall of dogs.

Transplantation to Irradiated Hosts: (A) A group of 4 normal dogs received 350 r single dose irradiation to the whole body and two

days later minced homologous dog embryos were transplanted to the anterior abdominal wall and the anterior chamber of each eye. (B) A group of 4 pregnant dogs less than half way through the period of gestation had their embryos removed aseptically, received 350 r single dose irradiation to the whole body immediately thereafter and then received transplants of minced autologous embryos to the anterior chamber of the eyes and the anterior abdominal wall. (C) A group of 4 normal dogs received 350 r single dose irradiation to the whole body, and two days later fresh minced beef embryo spleen was trans-

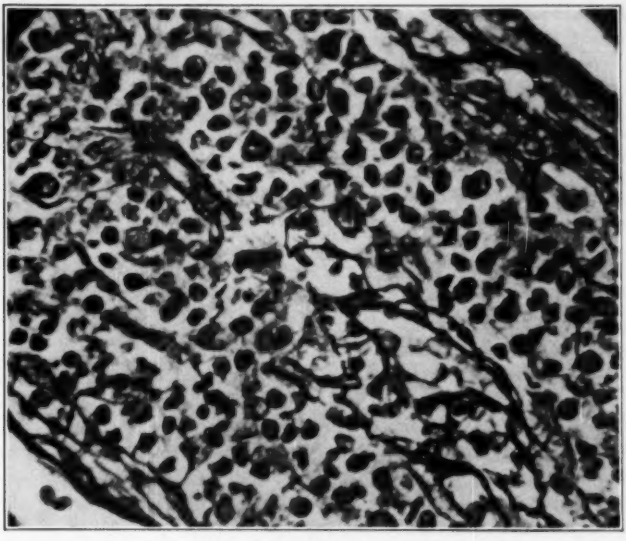

Fig. 21.—Reticulum stain. × 650.

planted to the anterior abdominal wall and the anterior chamber of the eyes.

All irradiated hosts died within twenty-one days of irradiation, with the usual finding of irradiation intoxication. The transplants showed varied stages of degeneration or, in a few instances, cartilaginous proliferation but no evidence of proliferation of tissue of the hematopoietic system (fig. 19). In the nonirradiated hosts proliferating cartilage was frequently encountered in the transplant, while in several instances some stage of osteogenesis was observed and occasionally a suggestion of early marrow formation could be detected. This formation of cartilage and osteogenic tissue was noted with bone marrow transplants and

when a mixture of embryonic tissue was transplanted in autologous, homologous and heterologous grafts. Occasionally a follicle with a collection of lymphocytes in a reticulum was found (figs. 20 and 21).

Whereas these results indicate that embryonic bone marrow and hematopoietic tissues or mixed embryonic tissue is not readily transplantable, it must be borne in mind that these experiments are few in number and the anterior abdominal wall may not be a favorable site for transplantation. The work of Greene has demonstrated that successful transplantation of embryonic and malignant issues is dependent on a fairly large number of trials.[8a] Furthermore, this same investigator has demonstrated true lymph follicles in the transplant of embryonic tissue to the anterior chamber of alien hosts.[8d] The more favorable sites for transplantation are still under study, but it appears that the anterior chamber of the eye and possibly the perirenal region are more suitable for transplantation of alien tissues. The explanation for this predilection is wanting.

COMMENT

The feasibility of bone marrow transplantation is predicated on the thesis that after irradiation the damage to bone marrow is a direct injury and that such damage is the vital disturbance.

The available evidence indicates that the damage from irradiation is probably a direct one and not the result of a circulating toxin. Cross circulation studies,[2] transplantation of irradiated hematopoietic tissues [15] and shielding experiments support this viewpoint.[9b]

With selected types of irradiation the alterations in the peripheral blood elements appear to be a fair index of the clinical condition of the irradiated host. Morphologic studies strongly suggest that the alterations in the peripheral blood elements in general parallel the alterations in the hematopoietic tissues and the depression and recovery of the peripheral blood elements are a direct function of the destruction and regeneration of the primitive cells of the hematopoietic system.

Certain phases of the role of the bone marrow in blood formation appear well established. The erythrocytes and granulocytes arise and mature almost solely from this site except for a few areas of extramedullary myelopoiesis in the newborn and a few small areas in adults.[16] The formation of platelets is now believed to be solely from the megakaryocytes of bone marrow and other tissues.[17] Lymphocytes probably do not have their origin in the bone marrow but may be found there.[18]

15. Unpublished data of this laboratory.

16. Ask-Upmark, E.: Tumor Simulating Intrathoracic Heterotropia of Bone Marrow, Acta. radiol. **26**:425, 1945.

17. Tocantins, L. M.: Blood Platelets, Medicine **17**:155, 1938.

18. Drinker, C. K., and Yoffey, J. M.: Lymphocytes, Lymph and Lymphoid Tissue, Cambridge, Mass., Harvard University Press, 1941, p. 277.

The lymph nodes, the lymphoid tissue of the alimentary canal, the spleen and the thymus represent the predominant, if not the sole, sources of lymphocytes.[19] How much of the function of lymphocyte formation can be taken over by other tissues, such as the bone marrow, during a period of demand is not known. However, it is believed that germinal centers are not essential for lymphocyte formation since active multiplication of these cells occurs before birth at a time when centers are not present. Even when germinal centers have appeared, they are subject to cyclic changes.[20]

Conceivably, then, the restoration of the bone marrow would provide an opportunity for restoration of erythrocytes, granulocytes and thrombocytes in part, while the fate of the lymphocytes would remain unknown. However, it must be recognized that dysfunction of the alimentary tract following irradiation may play a significant role in irradiation blood dyscrasias.[12] Furthermore, the purpuric manifestations of irradiation may be associated not only with conspicuous thrombocytopenia but also with less well defined vascular dysfunction and hyperheparinemia.[21]

Although intramedullary transplantation of marrow is physiologically desirable, the experiments reported herein indicate that such a site is undesirable because of inaccessibility, extensive intramedullary bleeding with subsequent organization and fibrosis and the limited quantities of marrow that can be so transplanted.

Inasmuch as intramedullary transplantation of marrow has been found ineffectual, attention was directed to the induction of extramedullary myelopoiesis and its significance. Extramedullary myelopoiesis normally may be encountered in the newborn and as a rare pathologic phenomenon in the adult. This subject has been reviewed recently.[16]

The results following the transplantation of bone marrow intravenously invite unusual opportunities for speculation. These results are believed to be slightly favorable as reflected by the small difference in mortality, morbidity and the hematologic data between the groups receiving transplants and control groups of animals. Furthermore, after such transplantation the hosts did not exhibit evidence of sensitivity or toxicity, a finding constantly noted after the injection of other tissues or their extracts.[22] The hemograms showed a decreased depression of the

19. Drinker and Yoffey,[18] pp. 17 and 217.

20. Drinker and Yoffey,[18] p. 16.

21. Allen, J. G., and Jacobsen, L. O.: Hyperheparinemia: Cause of the Hemorrhagic Syndrome Associated with Ionizing Radiation, Science **105**:388, 1947. Rekers, P. E., and Field, J. B.: Control of Hemorrhagic Syndrome and Reduction in X-Radiation Mortality with a Flavonone, ibid. **107**:2766, 1948.

22. Winternitz, M. C.; Mylon, E., and Katzentstein, R.: Studies on the Relation of the Kidney to Cardiovascular Disease, Yale J. Biol. & Med. **13**:595, 1940.

nucleated cells, although the magnitude of the increase in the nucleated cell counts after injection was not as great as would be expected from the quantity of cells injected. It is believed that the slightly increased numbers of cells in circulation were the direct result of the injection rather than of a mobilization of cells such as monocytes. The intravenous administration of a particulate matter, such as india ink, to a similar group of irradiated animals failed to produce the same hematologic picture. Only rarely was a true marrow cell identified in the smear taken immediately after injection. This evidence, in conjunction with the pathologic finding in the lungs of calcified deposits in the pulmonary veins with a cellular proliferation, strongly suggests that the injected marrow is rapidly filtered out in the lungs.

Attempts at inducement of extramedullary myelopoiesis by transplantation of marrow into such sites as the subcutaneous, ocular, intramuscular or peritoneal regions resulted in small areas of bone formation. That bone formation, rather than calcific deposits, results from homologous marrow transplants is evident by the demonstration of bone lacunas (fig. 13).

Further work in this laboratory on dogs indicated that heterotopic bone can be produced readily from the transplantation of bladder mucosa to rectus fascia or the transplantation of rectus fascia to the bladder wall. However, this bone formation is not always accompanied with marrow, nor is it early enough or of sufficient magnitude to be of any benefit to animals suffering from acute irradiation intoxication.[15]

SUMMARY

1. Transplantation of normal marrow to intramedullary marrow sites is without appreciable benefit to the irradiated host. Such procedures induce intramedullary bleeding, with resultant organization and fibrosis rather than stimulation of bone marrow growth.

2. Transplantation of bone and marrow results in death and replacement of the graft. The newly formed bone marrow probably arises from persisting portions of the original marrow rather than from the transplanted marrow.

3. Transplantation of normal marrow to normal or irradiated spleen or liver is without appreciable benefit. Residual deposits of the marrow fat only can be demonstrated.

4. Stimulated bone marrow transplanted intravenously results in multiple heterotopic bone spicules within the pulmonary veins of the lungs. The evidence suggests that with this type of marrow transplanting the mortality is 43 per cent whereas the mortality in the control group is 67 per cent. Likewise the total white blood cell count and the absolute lymphocyte and the reticulocyte values of the peripheral blood are increased slightly in the group of animals receiving transplants.

5. Surgical procedures put an additional load on the irradiated host. However, these procedures do not appear to inhibit the formation of callus and subsequent bone growth.

6. An explanation for the inability to transplant bone marrow successfully was studied further. Such failure could not be adequately explained on the basis of lack of demand on the part of the recipient for bone marrow, homogeneity or selection of the site of transplant. The transplantation of bone marrow to such regions as the anterior chamber of the eye, the subcutaneous region, intramuscular regions, intraperitoneal sites and within the medulla of long bones was uniformly unsuccessful.

7. The belief that tissue sensitivity can be reduced and rendered more acceptable for transplantation by passing the tissue through culture mediums or subjecting the donor and/or host to irradiation is not supported by these studies.

8. Autologous or homologous marrow transplanted to extramedullary sites rapidly results in heterotopic bone formation.

9. Transplantation of selected autologous, homologous and heterologous hematopoietic embryonal tissues to irradiated hosts showed no evidence of alteration of the irradiation intoxication in these hosts or conclusive evidence of successful transplantation of these tissues in the short period of the study.

10. Transplantation of selected autologous, homologous and heterologous embryonal tissues to nonirradiated hosts and examination at least sixty days after frequently showed proliferating cartilage, some osteogenesis and occasionally a suggestion of early marrow formation.

ANOMALIES OF THE GALLBLADDER

Report of a Case of Left-Sided Floating Gallbladder

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CONGENITAL abnormalities and malpositions of the gallbladder are relatively rare, but since they are encountered occasionally in surgery of the biliary tract it is desirable for the surgeon to be familiar with them. Many types of anomalies of the gallbladder have been described. These include congenital reduplication of the gallbladder, bilobed gallbladder, anomalous positions of the gallbladder, "hourglass" deformities and congenital absence of the gallbladder.

The various types of congenital abnormalities of the gallbladder have been reviewed by several authors including Schachner,[1] Gross[2] and Meade.[3] In a review of the literature, Guyton[4] found only 40 cases of congenital reduplication of the gallbladder that had been proved at necropsy or at operation. For descriptive purposes, Boyden[5] has divided anomalies of this type into two groups: vesica divisa, or cleft gallbladder, which has two cavities emptying into a single cystic duct, and vesica duplex, which consists of two separate gallbladders, each with its own cystic duct. The accessory gallbladder arises from the cystic duct; 24 examples of this anomaly have been reported in the literature. Schachner[1] has described 1 case of double gallbladder in which one

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1. Schachner, A.: Anomalies of the Gall-Bladder and Bile-Passages, with the Report of a Double Gall-Bladder and a Floating Gall-Bladder, Ann. Surg. **64**:419-433 (Oct.) 1916.

2. Gross, R. E.: Congenital Anomalies of the Gallbladder: A Review of One Hundred and Forty-Eight Cases, with a Report of a Double Gallbladder, Arch. Surg. **32**:131-162 (Jan.) 1936.

3. Meade, H. S.: Congenital Abnormalities of the Gallbladder, Irish J. M. Sc., May 1944, pp. 161-162.

4. Guyton, W. L.: Double Gallbladder, Am. J. Surg. **72**:118-120 (July) 1946.

5. Boyden, E. A.: The Accessory Gall-Bladder—An Embryological and Comparative Study of Aberrant Biliary Vesicles Occurring in Man and the Domestic Mammals, Am. J. Anat. **38**:177-222 (Nov.) 1926.

vesicle was lying in the normal position under the right lobe of the liver and the accessory vesicle was attached to the under surface of the left lobe of the liver.

Complete absence of the gallbladder has been described by Gay,[6] Gross [2] and, more recently, Dixon and Lichtman,[7] who reported 10 cases of this anomaly observed at the Mayo Clinic.

Because of the frequent complications requiring surgical intervention that are produced by anomalous positions of the gallbladder, this group of abnormalities is considered to be the most interesting surgically. Malpositions may vary from that of an intrahepatic gallbladder completely buried in the substance of the liver to that of a free-floating gallbladder attached only by the cystic duct. Gallbladders in anomalous positions include intrahepatic, left-sided and floating gallbladders.

The intrahepatic type of gallbladder has been reviewed by Walter and Neiman,[8] McNamee [9] and Lane.[10] McNamee reported 27 cases; 14 of these involved infants in whom the condition was found at necropsy, and 13 involved adults. Lane,[10] in 1946, reported what he believed to be the first case of empyema of an intrahepatic gallbladder, which he treated by drainage after removing multiple stones. He stated that draining the intrahepatic gallbladder is preferable to performing a cholecystectomy, because the latter procedure usually produces severe hemorrhage. McNamee [9] reported 1 case in which fatal hemorrhage occurred as a result of removal of an intrahepatic gallbladder.

Walton [11] has observed that the left-sided gallbladder, unassociated with situs inversus viscerum, is one of the rarest anomalies of this organ. This unusual abnormality also has been described by Schachner,[1] Gross [2] and, more recently, McGowan, Nussbaum and Burroughs.[12] Gross [2] found only 7 cases reported in the literature, and McGowan [12] reported an additional case in his recent paper. According to these

6. Gay, R. J.: Developmental Anomalies of the Gallbladder: Report of a Case, Tr. Path. Soc., Chicago. **5**:108-113 (May 12 to June 9) 1902.

7. Dixon, C. F., and Lichtman, A. L.: Congenital Absence of the Gall Bladder, Surgery **17**:11-21 (Jan.) 1945.

8. Walter, O. M., and Neiman, A.: Case Report of an Intrahepatic Gall-Bladder in an Adult, with a Review of the Literature, Illinois M. J. **60**:478-480 (Dec.) 1931.

9. McNamee, E. P.: Intrahepatic Gallbladder, Am. J. Roentgenol. **33**:603-610 (May) 1935.

10. Lane, W. R.: Empyema of Intrahepatic Gall-Bladder: Report of a Case, Australian & New Zealand J. Surg. **15**:304-305 (April) 1946.

11. Walton, A. J.: Congenital Malposition of the Gall-Bladder, Lancet **1**:925-926 (April 6) 1912.

12. McGowan, J. M.; Nussbaum, C. C., and Burroughs, E. W.: Cholecystitis Due to Giardia Lamblia in a Left-Sided Gallbladder, Ann. Surg. **128**:1032-1037 (Nov.) 1948.

authors, the gallbladder in each case was normal in size and was found lying on the under surface of the left lobe of the liver, to the left of the round and falciform ligaments. Under these conditions, the gallbladder may be hidden from the surgeon's view when the usual incision in the right upper quadrant is made. In Gross's [2] series, the cystic duct entered the left hepatic duct in 1 case and entered at the junction of the hepatic and common ducts in 3 cases.

A review of the clinical records of the anomalies of the gallbladder at the clinic revealed 1 case of a left-sided gallbladder, in which a man, 37 years old, complained of intermittent, severe, sharp pain under the right costal margin. When operated on, he had acute cholecystitis with beginning gangrene, and one stone was found in the cystic duct. The gallbladder was found lying to the left of the falciform ligament of the liver, apparently not in a notch but on the flat under surface of the left lobe of the liver. There were firm adhesions between the gallbladder and the left lobe of the liver.

The mobile, or floating, gallbladder has been described by many authors, including Schachner,[1] Gross,[2] Meade,[3] Short and Paul,[13] Barber [14] and Meeker and Lisenby.[15] Whereas the gallbladder normally lies in the gallbladder notch of the liver and is held in place by reflected peritoneum, the floating gallbladder is completely invested with peritoneum and is attached to the liver by only a short mesentery. Meade [3] reported 1 case, that of a woman 54 years of age, in which the gallbladder and cystic duct were completely invested with peritoneum, without evidence of a mesentery. The only attachment for the gallbladder was at the point where the cystic duct joined the common duct. More frequently the gallbladder hangs from the liver by a short mesentery which may vary from one attached to the gallbladder and cystic duct to one supporting only the cystic duct. As a result of the mobility permitted by the short mesentery, the gallbladder may become twisted on itself and produce torsion of sufficient degree to interrupt the blood supply of the organ. The finding of a gallbladder with a mesentery is not unusual. Brewer,[16] in an analysis of 100 dissections, found 5 instances in which the gallbladder was permitted considerable mobility because of a distinct mesentery formed by a double fold of peritoneum. Short

13. Short, A. R., and Paul, R. G.: Torsion of the Gall-Bladder, Brit. J. Surg. **22**:301-309 (Oct.) 1934.

14. Barber, A. H.: Acute Torsion of the Gall-Bladder, Brit. M. J. **2**:1272-1273 (Dec. 30) 1939.

15. Meeker, W. R., and Lisenby, J. O.: Ptosis and Torsion of the Gall-Bladder, South. M. J. **25**:609-614 (June) 1932.

16. Brewer, G. E.: Preliminary Report on the Surgical Anatomy of the Gall-Bladder and Ducts from an Analysis of One Hundred Dissections, Ann. Surg. **29**:721-730, 1899.

and Paul [13] pointed out that mobility of the gallbladder depends not so much on the mesentery as it does on a short mesenteric attachment. Barber [14] stated that although a gallbladder with a mesenteric attachment is allowed considerable movement a complete axial rotation can take place only when the gallbladder is completely invested with peritoneum and hangs free in the abdomen.

The floating gallbladder is a developmental anomaly. The liver and biliary tract are formed as a diverticulum from the ventral surface of the foregut, and the gallbladder and cystic duct develop as an evagination from the original diverticulum. Normally, the gallbladder is attached to the liver and held in place by peritoneum reflected over it from the liver so that only a small portion of the fundus lies below the level of the anterior border of the liver. However, occasionally the cystic duct becomes so elongated that the entire gallbladder hangs below the anterior border of the liver, in which case the latter is completely enclosed by peritoneum.

The floating gallbladder is of special interest surgically because of the possibility of the occurrence of torsion which demands emergency surgical management. Torsion of the gallbladder was first described in 1898 by Wendel,[17] who published a graphic and lucid account of the clinical course and of the preoperative and operative findings in a case of floating gallbladder complicated by torsion. Prior to the development of torsion, the gallbladder in this case had been palpated in the left lumbar region on one occasion and in the right lower quadrant at a later examination. At the time of operation the cystic duct measured 3¼ inches (8.3 cm.) in length, which explained the unusual mobility of this organ.

Gross [2] has collected reports of 50 cases of torsion of the gallbladder. In his series, 84 per cent of the patients were females and 16 per cent were males. The average age was 59 years. Fifty per cent of the patients were between the ages of 60 and 80 years, but the largest group, by decades, was that of patients between the ages of 70 and 80 years.

Short and Paul [13] reviewed a group of 50 reported cases of torsion of the gallbladder and added 3 of their own cases in which they had operated in a four year period. These authors have observed that some of the patients showed evidence of gallbladder disease, such as pain in the right upper quadrant and qualitative food intolerance, but rarely jaundice, while others enjoyed unbroken good health until torsion of the gallbladder occurred.

17. Wendel, A. V.: A Case of Floating Gall-Bladder and Kidney Complicated by Cholelithiasis with Perforation of the Gall-Bladder, Ann. Surg. **27**:199-202 (Jan.-June) 1898.

The occurrence of torsion of the gallbladder produces rather constant signs and symptoms. There is a sudden onset of intense colicky pain in the right upper quadrant which persists but rarely extends to the back or right shoulder. Vomiting usually is present and urgent. Physical examination usually reveals an elderly patient, most commonly a woman, with tenderness and spasm in the right upper quadrant. Jaundice is usually not detected. Gross [2] reported that in 54 per cent of cases the gallbladder may be palpated, usually just below the liver, but it may be found in other parts of the abdomen.

Husband and Schmitt [18] have stated that torsion of the gallbladder is a rare finding, since only about 80 cases have been reported. Gowland [19] added 1 case report of this anomaly in 1946. However, in spite of the infrequency of this abdominal emergency, Short and Paul [18] and Husband and Schmitt [18] suggested that a preoperative diagnosis of torsion of the gallbladder should be considered when an elderly woman who has been well previously suddenly has severe, persistent pain in the right upper quadrant with nausea and vomiting, abdominal tenderness and spasm and a tender mass palpable in the right upper quadrant.

At operation for torsion of the gallbladder, the vesicle usually is found twisted on its pedicle, with compression of the cystic artery and vein, so that the wall of the gallbladder is edematous and necrotic. In the cases reported by Barber,[14] Gross [2] and Meade,[8] the gallbladder was twisted on the cystic duct anywhere from 90 to 360 degrees in a clockwise direction, and hemorrhagic fluid usually was found in the peritoneal cavity.

In a review of the clinical records and necropsy reports at the Mayo Clinic, record of only 1 case of floating gallbladder was found. The patient was a woman aged 38 years. The gallbladder was rudimentary but pendulous and was without attachment to the liver except by the cystic duct.

Our interest in anomalies of the gallbladder was stimulated by the finding by one of us (C. W. M.) of a left-sided floating gallbladder.

REPORT OF A CASE

A white woman, 56 years of age, was first seen at the clinic on Dec. 6, 1937, at which time her chief complaints were urinary incontinence and abdominal discomfort. She stated that she had had frequent spells of bloating and abdominal discomfort after meals. She felt as though belching might relieve her, but she had been unable to belch. There had been no nausea, vomiting or qualitative

18. Husband, C. W., and Schmitt, N. L.: Torsion of the Gallbladder Associated with Acute Appendicitis, J. Internat. Coll. Surgeons **8**:348-351 (July-Aug.) 1945.

19. Gowland, M. M.: Acute Volvulus of the Gallbladder, Canad. M. A. J. **54**:485 (May) 1946.

intolerance to food at that time. Jaundice had not been present. Since her most pressing complaint was urinary incontinence, she was operated on for the correction of this condition, and then she returned to her home. She came back to the clinic on Dec. 3, 1948, because her symptoms of abdominal discomfort had increased progressively since 1943. She complained of bloating and crampy pains in the upper part of the abdomen after each meal or with the ingestion of any type of food. For several months prior to admission she frequently had spit up small amounts of watery fluid but had not actually vomited. In the middle of November 1948 nausea and vomiting had developed; it usually appeared two to three hours after the noon meal. On November 29 she had had a sudden onset of severe, sharp pain in the midportion of the epigastrium which "doubled her up," but the pain had lasted only a short time. After this attack, she had had soreness in the right subcostal region.

On her admission, in December 1948, she complained of sharp intermittent pain in the epigastrium which was increased by deep breathing. Vomiting relieved the pain temporarily, but it recurred after each meal. She said her stools had been light in color since the attack of severe pain three weeks prior to her admission. Her normal weight was 183 pounds (83 Kg.), but her weight at the time of admission was 158 pounds (71.7 Kg.). There was tenderness, grade 1, in the epigastrium and the hypochondrium, but no mass could be felt and jaundice was not detectable.

Cholecystectomy was performed on December 11, a preoperative diagnosis of chronic cholecystitis with cholelithiasis having been made. The abdomen was opened by means of a primary upper right rectus incision. On first inspection it appeared that there had been a shift in position of the gallbladder from the right to the left lobe of the liver because the round ligament lay to the right of the gallbladder and the falciform ligament inserted between the right and left lobes, about an inch (2.5 cm.) to the right of where the gallbladder was lying. The gallbladder was not attached to the right or left lobes, but rather it was free-floating, with a small posteriorly situated mesentery through which ran the cystic artery. The cystic duct and the gallbladder were invested with peritoneum. The former was 6 cm. long and emptied into the common duct. The gallbladder contained a single stone which measured 1.5 cm. in diameter. The liver showed grade 1 hepatitis. The patient had an uneventful postoperative course.

HETEROTOPIC PANCREATIC TISSUE

Report of a Case Presenting Symptoms of Ulcer and Review of the Recent Literature

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THE TERM "heterotopic pancreatic tissue," currently favored by Barbosa, Dockerty and Waugh [1] to describe the condition of an anatomically separate mass of pancreatic tissue in an ectopic position, is not universally adhered to in the literature, which made the recent count of the number of described cases difficult. Although the medical history of this condition reaches back to 1727, when Jean Schultz has been given credit for first having described this condition without the aid of microscopic confirmation,[2] and to 1859, when Klob made the first histologic study of 2 cases, it was in 1903 that Magnus-Alsleben [3] reported a series of five "adenomyomata" of the stomach and described alveoli of Brunner's glandular, pancreatic and undifferentiated types surrounded by smooth muscle masses, thereby focusing attention on the possibility of a gradation of differentiation of these ectopic masses. In 1909 Gruzdeff [4] described an "adenomyoma" which produced clinical symptoms, though no pancreatic epithelium was noted. Lauche,[5] in 1924, reserved the term "adenomyoma" for pancreatic heterotopias, without differentiation of the epithelial elements. In this paper he classified all heterotopic tissues. The following year Stewart and Taylor [6] described 4 cases showing Brunner's glandular, pancreatic and

1. (*a*) Barbosa, J. J. de C., and Waugh, J. M.: Heterotopic Pancreatic Tissue, Clinically Significant in the Gastric Wall of a Boy Six Years of Age, Proc. Staff Meet., Mayo Clin. **22**:25-30 (Jan. 22) 1947. (*b*) Barbosa, J. J. de C.; Dockerty, M. B., and Waugh, J. M.: Pancreatic Heterotopia: Review of the Literature and Report of Forty-One Authenticated Surgical Cases, of Which Twenty-Five Were Clinically Significant, Surg., Gynec. & Obst. **82**:527-541 (May) 1946.

2. Hunt, V. C., and Bonesteel, H. T. S.: Meckel's Diverticulum Containing Aberrant Pancreas, Arch. Surg. **28**:425-439 (March) 1934.

3. Magnus-Alsleben, E.: Adenomyome des pylorus, Virchows Arch. f. path. Anat. **173**:137-156 (July) 1903.

4. Gruzdeff, D. A.: Rare Case of Adenomyoma of the Stomach, with Heterotype of the Epithelium of the Mucosa, Med. Obozr., Mosk. **71**:805-811, 1909.

5. Lauche, A.: Die Heterotopien der ortsgehöregen Epithels im Bereich des Verdauungskanals, Virchows Arch. f. path. Anat. **252**:39-88, 1924.

6. Stewart, M. J., and Taylor, A. L.: Adenomyoma of the Stomach, J. Path. & Bact. **28**:195-202, 1925.

undifferentiated types of epithelium and utilized the classification of Lauche. In 1928 Woolsey and Millzner [7] concurred with the usage of the term "adenomyoma" to describe heterotopias of the gastrointestinal tract and ascribed this term to those lesions presenting the undifferentiated type of epithelium. Clarke,[8] in 1940, is given recognition for initiating the term "myo-epithelial hamartoma of the gastro-intestinal tract" in referring to these ectopic pancreatic masses. Clarke described 8 cases, only 1 of which presented acini of the pancreatic type exclusively, the remainder being divided into less differentiated types, "adenomyoma" and "incompletely differentiated aberrant pancreas." Mitchell and Angrist,[9] writing in 1943, instanced 24 cases to justify the use of the term "myoepithelial hamartoma." Of these, 11 were termed cases of "aberrant pancreas" while 13 were designated as cases of "adenomyoma." The review articles of Warthin,[10] Horgan,[11] Ritter,[12] Simpson,[13] Hunt and Bonesteel,[2] Poppi,[14] Branch and Gross,[15] Faust and Mudgett,[16] Present [17] and Barbosa, Dockerty and Waugh [1] are all excellent, but because of the variance in nomenclature and the consequent omission of cases from recent reviews, it was thought desirable to collect cases not included in the foregoing reviews and cases published since the comprehensive review through March 1944 by Barbosa, Dockerty and Waugh. These, together with a case which has recently come to our attention, are presented herewith.

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7. Woolsey, J. H., and Millzner, R. J.: Adenomyoma of the Stomach, Arch. Surg. **16**:583-592 (Feb.) 1928.

8. Clarke, B. E.: Myoepithelial Hamartoma of Gastrointestinal Tract: Report of Eight Cases with Comment Concerning Genesis and Nomenclature, Arch. Path. **30**:143-152 (July) 1940.

9. Mitchell, N., and Angrist, A.: Myo-Epithelial Hamartoma of the Gastrointestinal Tract (Clarke), Ann. Int. Med. **19**:952-964 (Dec.) 1943.

10. Warthin, A. S.: Two Cases of Accessory Pancreas (Omentum and Stomach), Phys. & Surg. **26**:337-351, 1904.

11. Horgan, E. J.: Accessory Pancreatic Tissue: Report of Two Cases, Arch. Surg. **2**:521-534 (May) 1921.

12. Ritter, L.: Zum klinischen Bilde und Sitz versprengter Pankreaskeime, Beitr. z. klin. Chir. **124**:157-172, 1921.

13. Simpson, W. M.: Aberrant Pancreatic Tissue: Analysis of One Hundred and Fifty Human Cases with Report of New Case, Warthin Ann. Vol., 1927, pp. 435-459.

14. Poppi, A.: Sui pancreas aberranti: (Rivista sintetica completa e contributo casistico), Arch. ital. d. mal. d. app. diger. **4**:534-579 (Dec.) 1935.

15. Branch, C. D., and Gross, R. E.: Aberrant Pancreatic Tissue in the Gastro-Intestinal Tract: A Report of Twenty-Four Cases, Arch. Surg. **31**:200-224 (Aug.) 1935.

16. Faust, D. B., and Mudgett, C. S.: Aberrant Pancreas with Review of the Literature and Report of a Case, Ann. Int. Med. **14**:717-728 (Oct.) 1940.

17. Present, A. J.: Aberrant Pancreas, Am. J. Roentgenol. **56**:55-57 (July) 1946.

REPORT OF A CASE

A white married man, aged 59 years, first presented himself at the Mayo Clinic for examination on Nov. 26, 1947, because of a pain in the epigastrium and the left upper quadrant of the abdomen which had been present for three years. The patient's family history was noncontributory. He had had malaria as a boy. His only operation had been a tonsillectomy eighteen years prior to his admission. Twelve years prior to admission he had had a "hemorrhage in his right eye," leaving no visual loss, and five years before his admission he had suffered from a sacroiliac strain which continued to cause him discomfort after exercise. For years he had had an "acid condition" of his stomach, relieved by sodium bicarbonate or milk. In 1929 his local physician had diagnosed a duodenal ulcer, associated with pylorospasm and a "spot" in his stomach observed on roentgenologic examination. He was placed on a strict ulcer regimen, and the ulcer, observed roentgenoscopically, was seen to heal; yet the lesion in his pylorus did not disappear. He was free from pain until three years before his entry to the hospital (1944), when he noted a return of the intermittent gnawing epigastric distress which came on two or three hours after meals and was relieved by food and antacids, as formerly. In 1946 a diagnosis of chronic appendicitis was made but no operation was performed. In July 1947 roentgenologic examination showed a "definite duodenal ulcer, also a prepyloric filling defect on the greater curvature and partly posterior," both on roentgenograms and by roentgenoscopy. Despite the ulcer, his concentration of hemoglobin was 100 per cent of normal, the remainder of the roentgenologic examinations of the gastrointestinal tract showed a normal condition and, aside from slight obesity, the results of the physical examination were not remarkable. He was again placed on an intensive ulcer regimen by his local physician, and after two weeks renewed roentgenologic examination showed marked improvement in the duodenal deformity but the filling defect in the prepyloric region remained as before. Again in November 1947 roentgenoscopy was performed, and the duodenum was found to be normal while the gastric defect remained. The patient was then symptom free but was sent to the clinic because of the persistence of the prepyloric defect, which his local physician felt to be caused by a benign lesion requiring surgical intervention.

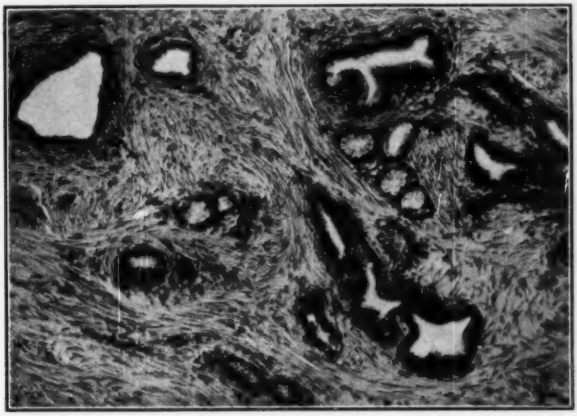
On admission to the clinic the physical examination revealed an obese white man weighing 212 pounds (about 96 Kg.) who presented no further remarkable findings, although, because of the adiposity, accurate examination of the abdomen was not possible.

Laboratory examination showed a hemoglobin concentration of 13.2 Gm. per hundred cubic centimeters of blood, and there were 4,680,000 erythrocytes and 9,000 leukocytes per cubic millimeter of blood. Examination of gastric contents after a test meal revealed 64 units of free hydrochloric acid and 80 units of total acid. The results of urinalysis, serologic tests, chemical examination of the blood, liver function tests, the sedimentation rate and roentgenograms of the chest were all within normal limits. A roentgenogram of the stomach showed a "small tumor about 2 inches [5 cm.] in diameter on the greater curvature in the antrum. An intramural tumor such as a leiomyoma is a possibility, although malignancy cannot be excluded." Exploration was recommended.

The roentgenologist and the medical and surgical consultants were all of the opinion that the lesion was benign but that malignancy could not be ruled out and consequently exploration was advisable. Surgical intervention was performed on Dec. 10, 1947, at which time a submucosal tumor 1 cm. in diameter was found on

the greater curvature of the stomach, 2.5 cm. above the pylorus. There was thickening of the pyloric sphincter and the musculature of the lower third of the stomach, presumptive evidence that there had been prolapse of the tumor through the pylorus, producing intermittent pyloric obstruction. Segmental excision of this region was carried out, and the anterior portion of the pyloric sphincter was divided. The duodenum was examined for an ulcer, as was the lower third of the stomach, but none was found. Reconstruction by gastroduodenostomy of the Heineke-Mikulicz type was performed. The gallbladder emptied readily, and no stones were palpated. The liver was normal. Careful palpation of the stomach at completion of the operation did not reveal any tumors.

The pathologist on examination of tissue from the stomach diagnosed the tumor as a pancreatic rest (so-called adenomyoma), 8 mm. in diameter and causing hypertrophy of the muscularis propria (figure). Leading down to this rest were two



Brunner's glandular acini, together with dilated ducts, surrounded by bundles of smooth muscle. From nodule removed from pyloric region of stomach in case presented herein; × 95.

mucosal diverticula, each 1.5 cm. in length. A node from the greater curvature of the stomach was inflammatory.

The postoperative convalescence was uneventful, and the patient was dismissed, to go home, on Dec. 23, 1947. A note from his physician a month later revealed that he was feeling well, and a letter from the patient two and a half months later stated that he was well and completely relieved of his dyspepsia.

COMMENT

In the light of recently published and previously unemphasized articles on this subject, some comment on this case is perhaps warranted.

The incidence of heterotopic pancreatic tissue has been estimated at between 0.55 and 5.6 per cent in necropsy material and as occurring in

Cases of Accessory Pancreas in Literature

Year	Author	Stomach	Duodenum	Jejunum	Ileum	Around Pancreas	Meckel's Diverticulum	Umbilical Region	Mesenteric Root	Gallbladder	Spleen	Liver	Omentum	Miscellaneous	Total
	Included in Article by Barbosa, Dockerty and Waugh Through March 1944	125	143	77	27	3	25	3	4	6	5	1	8	44	471
	Other Cases Prior to Article by Barbosa, Dockerty and Waugh														
1928	Woolsey and Millzner [7]	1	..	..	..	..	..	..	..	..	..	..	..	..	1
1938	Andersen [27]	..	..	1	..	..	..	..	..	..	..	..	..	..	1
1938	Thomas, J., and Schlutz, F. W.: Am. J. Dis. Child. **56**: 336 (Aug.) 1938	..	..	1	..	..	..	..	..	..	..	..	..	..	1
1940	Clarke [5]	4	1	1	..	..	1	..	..	1	..	..	..	..	8
1941	Mallet-Guy and Marion [24a]	..	1	..	..	..	..	..	..	..	..	..	..	..	1
1941	Desjacques, M.: Lyon med. **167**: 34 (Jan.) 1942	1	..	..	..	..	..	..	..	..	..	..	..	..	1
1942	Garin and Coudert [33]	1	1	..	..	..	..	..	..	..	..	..	..	..	2
1943	du Bourguet and Berge [26]	1	..	..	..	..	..	..	..	..	..	..	..	..	1
1943	Mitchell and Angrist [9]	4	5	2	4	1	1	..	..	7	..	..	..	..	24
1944	Marshall and Aronoff [19]	..	..	..	..	..	..	..	..	..	..	..	..	3	3
	Total	12	8	5	4	1	2	..	..	8	..	..	..	3	43
	Cases Since Article by Barbosa, Dockerty and Waugh														
1944	Brown, Flachs and Wasserman [31]	..	1	..	..	..	..	..	..	..	..	..	..	..	1
1944	Young [32]	..	..	..	..	..	..	..	..	..	..	..	1	..	1
1944	Troll [22]	..	..	..	1	..	2	..	..	..	..	..	..	..	3
1945	Baylin [36]	..	1	..	..	..	..	..	..	..	..	..	..	..	1
1946	Martins [24b]	..	..	1	..	..	..	..	..	..	..	..	..	..	1
1946	Waugh and Harding [18]	3	2	..	..	..	..	..	..	..	..	..	..	..	5
1946	Garre, Latienda and de Dominicis: Arch. argent. de enferm. d. ap. digest y. de la nutrición **21**: 264-273 (May-June) 1946	..	1	..	..	..	..	..	..	..	..	..	..	..	1
1946	Norris [34]	..	1	..	..	..	..	..	..	..	..	..	..	..	1
1946	Present [17]	2	..	..	..	..	..	..	..	..	..	..	..	..	2
1946	Russo [27b]	..	1	2	..	..	..	..	..	..	..	..	..	..	3
1946	Kalfayan [29]	..	1	..	..	..	..	..	..	..	..	..	..	..	1
1946	Mutschmann, P. N.: Am. J. Surg. **72**: 282 (Aug.) 1946	..	..	..	..	..	..	..	..	1	..	..	..	..	1
1946	Collett [25]	1	..	..	..	..	..	..	..	..	..	..	..	..	1
1946	Roach and Poppel [30]	3	..	..	..	..	..	..	..	..	..	..	..	..	3
1947	Barbosa, Dockerty and Waugh [1b]	1	..	..	..	..	..	..	..	..	..	..	..	..	1
1947	Hallendorf, L. C., and Lovelace, W. R.: Proc. Staff Meet., Mayo Clin. **22**: 53 (Feb. 5) 1947	..	..	..	..	..	1	..	..	..	..	..	..	..	1
1947	Chapman, Vogel and Schomaker [34c]	1	..	..	..	..	..	..	..	..	..	..	..	..	1
	Total	11	8	3	1	..	3	..	..	1	..	..	1	..	28
	Present case	1	..	..	..	..	..	..	..	..	..	..	..	..	1
	Grand total	149	159	85	32	4	30	3	4	15	5	1	9	47	543

1 in 160 to 600 operations.[18] Besides the foregoing case, the total number of cases of heterotopic pancreatic tissue that we have been able to find in the literature since the review of Barbosa, Dockerty and Waugh is 28. In addition, we have been able to find 43 previously published cases, not reviewed by the foregoing authors. With the inclusion of our own case, this brings the total number to 543 (table). It is to be noted, however, that of the additional 71 cases in the literature 3 are included which the author mentioned he had only observed, both confirmation and location being omitted.[19]

The location of heterotopic pancreatic tissue has been noted in the stomach, duodenum or jejunum in about 70 per cent of the cases.[20] In the series being reported, 72 per cent of the lesions were found in these regions. About a fourth of these heterotopias have been found in the stomach, and in this regard the lesion in our case presented in a common site. In the recent literature several cases have been reported in which the gallbladder was the site of the tumor.

Recently, the question of etiology has not been further elucidated, but it is interesting that the case presented herein was illustrative of the coexistence of diverticula and heterotopic pancreatic tissue, a situation investigated by Bolognesi,[21] who produced diverticula in the duodenum of dogs by the implantation of pancreatic tissue. Troll [22] has commented on the relatively high incidence of this lesion in Meckel's diverticula and has suggested that this may be due to the lability of the fetal intestinal tissue during the inception of this viscus, as emphasized by the variability of the size and location of this diverticulum.

Pathologically, this case presented the type of lesion referred to by Clarke [8] as an adenomyoma, inasmuch as no pancreatic acini were recognized per se; rather, the picture was microscopically that of Brunner's glandular acini and ducts, surrounded by smooth muscle. Lauche [5] classified heterotopic tissue as (1) acquired, either (*a*) regenerative or (*b*) hyperplastic and (2) congenital, either (*a*) atavistic or (*b*) dysontogenetic. Stewart and Taylor [6] utilized this classification to label their 4 cases under the fourth type, thereby also making the assumption that the lesions are of a developmental origin. Clarke [8] carried through with

18. Waugh, T. R., and Harding, E. W.: Heterotopic Pancreatic Tissue in the Region of the Pyloric Orifice: A Radiological and Pathological Analysis of Five Cases of Clinically Suspected Peptic Ulcer in Which Only Pancreatic Rests Were Found, Gastroenterology **6**:417-435 (May) 1946. Barbosa and Waugh.[1a]

19. Marshall, S. F., and Aronoff, B. L.: Symposium on Gastrointestinal Surgery: Tumors of Stomach, S. Clin. North America **24**:607-617 (June) 1944.

20. Barbosa and Waugh.[1a] Woolsey.[7]

21. Bolognesi, G.: Le pancréas accessoire: Contribution clinique, Arch. d. mal. de l'app. digestif. **23**:708-745 (July) 1933.

22. Troll, M. M.: Aberrant Pancreatic and Gastric Tissue in the Intestinal Tract, Arch. Path. **38**:375-380 (Dec.) 1944.

this idea in labeling the lesions myoepithelial hamartomas of the gastrointestinal tract and divided them into three groups according to the degree of differentiation of the epithelial elements: (1) aberrant pancreas, showing acini of pancreatic type; (2) adenomyoma, exhibiting some acini which were undifferentiated and others of Brunner's gland type; (3) incompletely differentiated aberrant pancreas, having some, but not all, of the acini of the pancreatic type, the remainder being either undifferentiated or of Brunner's gland type.[6] No continuity with the crypts of Lieberkühn was noted in this case, as has been described by Nicholson,[23] nor was there ulceration or mucous cell metaplasia of gastric glands of the overlying mucous membrane. The tumor in this case was in the submucosa, and the muscularis propria was greatly thickened, coinciding with findings previously reported.[24] The surgeon noted that this benign tumor may well have been capable of prolapse through the pylorus, as attested by the hypertrophy of the muscle, a condition reported by several authors.[25] The surgeon did not speculate on the presumptive diagnosis from the gross pathologic features of the tumor, a possibility advanced by some,[26] but final diagnosis awaited histologic examination, as emphasized by others.[16]

Comments in the later literature with regard to the possible pathologic complications which may occur mention cyst formation, acute and chronic pancreatitis, hemorrhage, necrosis, abscess formation, atrophy, pyloric and biliary obstruction, multiple tumors, malignant degeneration, endocrine functioning or any change which may occur in the anatomic pancreas. Changes in the aberrant pancreatic tissue synchronous with identical changes in the anatomic pancreas have been noted.[27]

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23. Nicholson, G. W.: Studies on Tumor Formation, Guy's Hosp. Rep. **73**:37-64, 1923.

24. (*a*) Mallet-Guy, M. M., and Marion, P.: Pancréas aberrant de la première portion du duodénum, Lyon chir. **37**:380-384 (May) 1941. (*b*) Martins, M.: Pancreas aberrante, Bol. San São Lucas **7**:115-120 (Feb.) 1946. (*c*) Chapman B. M.; Vogel, W. F., and Schomaker, T. P.: Massive Gastric Hemorrhage Associated with Aberrant Pancreas in Stomach, Gastroenterology **8**:367-374 (March) 1947. (*d*) Barbosa and Waugh.[1a]

25. Collett, R. W.: Prepyloric Polypus in Stomach of Child Diagnosed Histologically as Aberrant Pancreatic Tissue: Report of a Case and Review of the Literature, Am. J. Dis. Child. **72**:545-551 (Nov.) 1946. Toland, C. G., and Kroger, W. P.: Myoma of the Stomach, West. J. Surg. **46**:259-266 (May) 1938. Weinberg, T. B., and Raider, L.: Pedunculated Tumors of the Stomach Prolapsing Through the Pylorus, Radiology **41**:52-55 (July) 1943.

26. du Bourguet and Berge: Pancréas accessoire pylorique, Mém. Acad. de chir. **68**:330-331 (Oct. 14) 1942.

27. (*a*) Andersen, D. H.: Cystic Fibrosis of the Pancreas and Its Relation to Celiac Disease, Am. J. Dis. Child. **56**:344-399 (Aug.) 1938. (*b*) Russo, M.: Tre casi di pancreas aberrante (contributo clinico), Gior. di med. **3**:261-264 (July-Aug.) 1946.

No clarification of the symptomatology of this condition has been evolved, as testified in the recent literature by emphasis on ambiguity or the absence of clinical features.[28] However, it has frequently been noted that symptoms of peptic ulcer may be simulated, as emphasized recently by Waugh and Harding.[18] In this paper 4 of the 5 cases presented ulcer-like symptoms, relieved by food and alkalis. These authors pointed out that the pain may be produced by heterotopic pancreatic tissue from (1) interference with the passage of food through the pylorus by the tissue masses, producing spasm of the stomach or the pylorus or both, (2) interference with the passage of peristaltic waves and resultant retention, (3) peptic ulceration from pancreatic enzymes being poured out from these masses and (4) malignant or benign tumor formation. In the case being presented the symptoms were those of peptic ulcer and the mechanism of the production of pain may have been on the basis of obstruction of the pylorus. It is also to be noted that there was free hydrochloric acid in this case, and, though this is usual, achlorhydria has been mentioned.[29] The diagnosis made from roentgenograms was that of benign tumor, a trend which continues to be supported by the later literature,[30] though some believe this medium to be equivocal.[18] Gastric retention of gallbladder dye drew attention to an obstructing lesion of this type in one report.[31]

In accord with previous reports on treatment of this condition, surgical exploration was performed, and the operation consisted of gastroduodenostomy preceded by local excision of the lesion. Young [32] reported a case in which only biopsy and ligation of the vessels supplying the lesion were carried out, whereupon he raised the question of the possible development of complications from this type of treatment. In not all cases will the lesion be found amenable to excision.[17]

The complications arising from the lesion in this case were those of partial obstruction by possible prolapse of the tumor through the pylorus and symptoms of peptic ulceration. In the recent literature, besides frequent reference to peptic ulceration,[33] mention has been made of

28. Present.[17] Waugh and Harding.[18] Mallet-Guy and Marion.[24a] du Bourguet and Berge.[26] Marshall and Aronoff.[19] Martins.[24b] Bolognesi.[21]

29. Kalfayan, B.: Duodenitis with Diverticulum and Ectopic Pancreatic Tissue, Arch. Path. **42**:228-231 (Aug.) 1946. Faust and Mudgett.[16]

30. Roach, J. F., and Poppel, M. H.: The Roentgen Demonstration of an Aberrant Pancreatic Nodule in the Stomach: Report of Three Cases, Am. J. Roentgenol. **56**:586-589 (Nov.) 1946. Present.[17]

31. Brown, S.; Flachs, K., and Wasserman, P.: Aberrant Pancreatic Tumor in the Duodenal Wall, Radiology **43**:385-386 (Oct.) 1944.

32. Young, H. B.: A Case of Accessory Pancreas in an Unusual Position Complicated by Acute Necrosis, Glasgow M. J. **142**:156-164 (Nov.) 1944.

33. Garin, and Coudert: Deux cas de pancréas aberrants avec ulcères gastro-duodénaux, Lyon méd. **167**:197-201 (March) 1942. Waugh and Harding.[18] Mallet-Guy and Marion.[24a]

gastroduodenitis,[29] carcinomatous degeneration,[34] hyperinsulinism,[35] hemorrhage,[29] obstructive jaundice,[36] intussusception,[18] obstruction [37] and even death.[29]

The prognosis is held to be good in cases in which the foregoing complications are not found, though cases have been observed in which the symptoms continued despite excision of the lesion.[16]

SUMMARY

A case of heterotopic pancreatic tissue is presented in which the lesion is classified as being of the adenomyoma type. With the presentation of this report, a total of 543 cases of this condition have been found in the literature. Comments on the case have been made in view of current reports on the subject.

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34. Norris, J. C.: Aberrant Pancreas in the Duodenum, South. M. J. **39**: 549-551 (July) 1946. Brown.[31] Nicholson.[28]

35. Norris.[34] Young.[32]

36. Baylin, G. J.: Aberrant Pancreatic Tissue as a Roentgenologic Problem, Am. J. Roentgenol. **53**:277-280 (March) 1945.

37. Krieg, E. G.: Heterotopic Pancreatic Tissue Producing Pyloric Obstruction: A Review and Case Report, Ann. Surg. **113**:346-370 (March) 1941. Mallet-Guy and Marion.[24a]

PHYSIOLOGIC AMPUTATION BY TOURNIQUET AND REFRIGERATION

Treatment of the Infected Gangrenous Extremity

ALFRED LARGE, M.D.
DETROIT

MANAGEMENT of the critically ill patient with moist gangrene of an extremity has always been a difficult problem. Treatment by the standard types of amputation with closure of the stump was abandoned years ago because the mortality was so high—often close to 100 per cent. Guillotine amputation with the stump left wide open was found to be much safer, the idea being to get rid of the gangrenous part as rapidly and simply as possible and to reamputate at a higher level when the patient's condition improved enough to warrant the procedure. But even with the protection afforded by the sulfonamide compounds and penicillin, such staged procedures have left much to be desired. Since the operative mortality has remained alarmingly high, investigations leading toward other more satisfactory methods of management of this critically ill group of patients have continued.

With the introduction of refrigeration anesthesia by Allen and Crossman,[1] it was hoped that the problem finally had been solved. This procedure involved cooling the involved extremity, thus producing anesthesia, and the application of a tourniquet, with resultant elimination of absorption from the gangrenous area. Later, after the patient's condition had improved sufficiently, amputation through the cooled tissues was performed without further anesthesia. Many surgeons adopted the technic of refrigeration anesthesia, but certain shortcomings of the method soon became apparent. Although the operative mortality as a rule was decreased to below 20 per cent, the wounds healed slowly,

From the Department of Surgery, Wayne University College of Medicine and the Detroit Receiving Hospital.

1. (*a*) Allen, F. M.: Resistance of Peripheral Tissues to Asphyxia at Various Temperatures, Surg., Gynec. & Obst. **67**:746-751 (Dec.) 1938. (*b*) Allen, F. M.: Reduced Temperatures in Surgery: I. Surgery of Limbs, Am. J. Surg. **52**:225-237 (May) 1941. (*c*) Crossman, L. W.; Allen, F. M.; Hurley, V.; Ruggiero, W., and Warden, C. E.: Refrigeration Anesthesia: Current Researches in Anesthesia and Analgesia **21**:241-254 (Sept.-Oct.) 1942. (*d*) Crossman, S. W.; Ruggiero, W. F.; Hurley, V., and Allen, F. M.: Reduced Temperatures in Surgery: II. Amputations for Peripheral Vascular Disease, Arch. Surg. **44**:139-156 (Jan.) 1942.

infection was seen frequently and gas gangrene of the stump has been reported.[2]

Because of the lack of accurate information about refrigeration, an experimental study of the effects of cooling on living tissues was undertaken and has been reported previously.[3] Briefly, wound healing and the spread of infection were studied, the dog being used as the experimental animal. The apparatus, which was devised by Bruneau and Heinbecker, permitted comfortable restraint of the animals and allowed the study of a cooled area in one forelimb, with the opposite forelimb used as control. It was found that (1) prolonged cooling delays wound healing, the degree of delay in healing being roughly proportional to the duration of the cooling period, (2) the resistance of tissues to bacterial invasion decreases after cooling; (3) the incidence of infection in wounds treated by delayed primary suture increases by refrigeration and (4) nerve degeneration follows prolonged cooling of an extremity.

It immediately became evident that the benefits of refrigeration, namely anesthesia and elimination of absorption from the part, could be obtained by cooling a gangrenous extremity and placing a tourniquet around the cooled area; it was equally clear that the deleterious effects of prolonged cooling just enumerated could be avoided by removing all the refrigerated tissues. On the basis of this, a simple method of physiologic amputation by tourniquet and refrigeration was developed for clinical use. It was suggested that ice and tourniquet be applied to a gangrenous limb below the site of proposed amputation in order to eliminate constitutional effects from the involved extremity. It was hoped that this would permit the patient's general condition to improve sufficiently so that amputation could be undertaken above the ligated and cooled area without undue risk. Early limited clinical experience with this physiologic type of amputation was gratifying. Fourteen critically ill patients, 6 of whom have been previously reported on,[4] showed rapid improvement and all survived after operation except for 1 who died as a result of strangulation obstruction of the small bowel which occurred during convalescence.[5] These encouraging results prompted further clinical trial, and it is with more recent results that this paper is primarily concerned.

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2. (*a*) Melick, D. W.: Refrigeration Anesthesia, Am. J. Surg. **70**:364-368 (Dec.) 1945. (*b*) Kirz, E.: Gas Gangrene After Amputation under Refrigeration Anesthesia: A Warning, Brit. M. J. **2**:662 (Nov. 18) 1944.

3. (*a*) Bruneau, J., and Heinbecker, P.: Effects of Cooling on Experimentally Infected Tissue, Ann. Surg. **120**:716-726 (Nov.) 1944. (*b*) Large, A., and Heinbecker, P.: The Effect of Cooling on Wound Healing, ibid. **120**:727-741 (Nov.) 1944. (*c*) Large, A., and Heinbecker, P.: Nerve Degeneration Following Prolonged Cooling of an Extremity, ibid. **120**:742-749 (Nov.) 1944.

4. Large, A., and Heinbecker, P.: Refrigeration in Clinical Surgery, Ann. Surg. **120**:707-715 (Nov.) 1944.

5. Heinbecker, P.: Personal communication to the author.

METHOD

Patients are carefully selected for treatment by refrigeration. Only the patient seriously ill with absorption from a gangrenous area, who obviously requires a major amputation and who must have it done at once to save his life, is treated by this method. Thus the procedure is limited to the few neglected cases of peripheral arterial occlusion in which there is progressive infection of an ischemic extremity, usually without the benefit of previous medical care or advice.

As soon as it is decided that refrigeration and tourniquet will be used, the level of subsequent amputation is determined. This is done, as in any other case of peripheral vascular disease requiring amputation, by clinical estimation of the adequacy of the circulation to the part (peripheral pulsations, level of cutaneous temperature change). It is important that the site of amputation be chosen before refrigeration is begun because the ice and tourniquet must be applied at a level well below the operative site so as not to interfere with subsequent wound healing. In actual practice, most patients have required supracondylar amputation. These

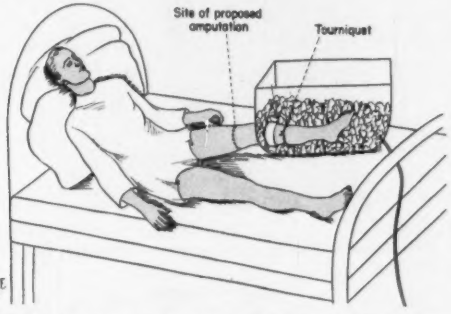

Fig. 1.—Drawing to show method of application of ice and tourniquet in a patient who will require supracondylar amputation. The ice is applied to a level just below the knee. This is not painful; on the contrary, rapid relief of pain from the gangrenous area is the rule. When anesthesia is obtained, usually after two to three hours, the tourniquet is applied as shown. Amputation is done above the cooled area when the patient's condition has improved sufficiently.

have been treated by the application of ice to a level just below the knee, and then, after anethesia has been obtained, a matter of two or three hours, the tourniquet is applied at a slightly lower level (fig. 1). With physiologic amputation by ice and tourniquet applied below the level of proposed operation in this manner, the patient's condition usually shows rapid improvement (figs. 2 and 3). When fever and all signs of toxicity have subsided, usually within twenty-four hours, amputation is performed under spinal or general anesthesia. The operation is done without a tourniquet, and short flaps or no flaps at all are made so as best to utilize the poor blood supply to the stump tissues usually found in arteriosclerotic patients. As already stated, supracondylar amputation has been done most frequently, and we have been impressed favorably by the conical circular amputation advocated by McKittrick[6] and others. The stump is closed without drainage.

6. McKittrick, L. S., and Pratt, T. C.: The Principles of and Results after Amputation for Diabetic Gangrene, Am. Surg. **100**:638-653 (Oct.) 1934.

Fig. 2 (case 21).—A 71 year old white diabetic male patient with moist gangrene of the foot illustrates the type of patient suitable for treatment by method advocated in this year.

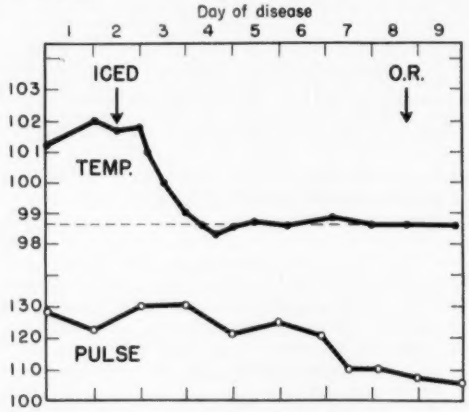

Fig. 3.—Temperature chart in case 21. The patient is toxic and semicomatose. Rapid improvement with application of ice and tourniquet occurred, as shown in chart. There was uneventful convalescence with primary wound healing after midthigh amputation.

In no case has the level of amputation been made higher by the use of ice and tourniquet. Indeed the converse has been true. For since spread of the gangrenous process is immediately halted by the application of ice and the tourniquet, the danger of progress upward of infection to the stump area is eliminated. Thus it has been possible to amputate these limbs at the lowest possible level consistent with adequate circulation to the stump.

RESULTS

During a recent seventeen month period, Jan. 1, 1947 to May 30, 1948, twenty-nine amputations in 27 patients have been performed by this method. Twenty-four of these amputations were performed at the Detroit Receiving Hospital and five at other institutions. The majority

TABLE 1.—*Amputation After Application of Tourniquet and Refrigeration*

Diagnosis	Number of Cases	Number of Amputations	Deaths
Diabetes with arteriosclerosis	15	16	1
Arteriosclerosis	7	7	..
Miscellaneous	5	6	1
Total	27	29	2
Mortality, percentage	7.4	6.9	...

TABLE 2.—*Types of Amputation After Refrigeration and Application of Tourniquet*

Type of Amputation	Number of Cases	Number of Amputations	Deaths
Lower, middle or upper part of thigh	10	10	..
Supracondylar	15	16	1
Midleg	1	2	..
Arm	1	1	1
Total	27	29	2
Mortality, percentage	7.4	6.9	...

of the patients were old and debilitated and had severe arteriosclerosis, often with diabetes mellitus (table 1), and all had some evidence of toxic absorption from the extremity. Most, but not all, showed a considerable elevation of temperature. Every patient improved markedly with physiologic separation of the gangrenous area by tourniquet and refrigeration and tolerated spinal or general anesthesia and operation itself without shock or other difficulty. The type of amputation performed is shown in table 2. There were 2 postoperative deaths, both at the Detroit Receiving Hospital. This is a mortality rate of 7.4 per cent. The first death was that of an 81 year old Negro woman with diabetes mellitus and cardiac decompensation, in whom infection in the stump and increasing evidence of cardiac failure developed, with death fourteen days after operation. The second death was that of a 65 year old white woman

with rheumatic heart disease, auricular fibrillation and a history of many embolic episodes. One of the latter resulted in gangrene of the left forearm, which began three weeks before her admission to the hospital. After physiologic amputation with ice and tourniquet, the arm was removed just above the elbow. The wound healed by first intention and the patient did well, only to die of a massive cerebral hemorrhage fourteen days after operation. Thus these 2 deaths were not directly related to operation or to the anesthetic agent used for the operation, but they occurred while the patients still were in the hospital and, therefore, are recorded as operative mortalities.[7]

COMMENT

Most patients with peripheral vascular disease are aware of the dangers of trauma and infection to their ischemic extremities and are able to obtain competent and continued medical care. Thus the far advanced neglected case of gangrene is infrequently observed today,

TABLE 3.—*Major Amputations at Detroit Receiving Hospital from Jan. 1, 1947 to May 31, 1948*

	Number of Cases	Number of Amputations
Total amputations	53	55
Number of amputations after use of tourniquet and refrigeration	23, or 43%	24, or 44%

in either hospital or office practice. That the problem does exist, however, is illustrated by the figures presented in this paper. During 1947 and the first five months of 1948, there were performed at the Detroit Receiving Hospital fifty-five major amputations for all causes. Twenty-four (44 per cent) of these were done on patients sick enough to require physiologic amputation by means of refrigeration and tourniquet (table 3).

The mortality for amputations after refrigeration may be compared to that for major amputations at the Detroit Receiving Hospital during 1940 and 1944, as shown in table 4. The former shows a favorable rate even though it is compared with the over-all mortality for amputation in previous years and not with the more truly comparable mortality among patients critically ill from toxic absorption, a figure previously greater than 50 per cent. This point is particularly important, as shown in table 5. In 1944 refrigeration was used for anesthesia in the most seriously ill patients but with poor results. It is evident that the patients treated by the method advocated in this discussion were

7. Since the preparation of this paper, 2 other patients in the series are known to have died of other causes.

benefited so markedly by physiologic separation of the diseased tissues from the body that the risk of amputation was reduced to a minimum, and the patients were given the usual types of anesthesia.

The fundamental principle underlying the rationale of physiologic amputation by tourniquet and refrigeration rests on the knowledge that the moment a tourniquet is applied to a limb amputation is in reality performed so far as the constitutional effects are concerned. This fact was appreciated by many during the First World War, and more recently Maxeiner [8] and Adolph [9] have advocated such "temporary tourniquet amputation." Refrigeration is employed only to permit painless application of the tourniquet and to prevent decomposition of already dead

TABLE 4.—*Major Amputations at Detroit Receiving Hospital*

Date	Number of Cases	Number of Amputations	Deaths	Percentage
Total amputations, 1940	23	28	6	20
Total amputations, 1944	39	40	10	26
Amputation after refrigeration, 1/1/1947 to 5/31/1948	23	24	2	8.7

TABLE 5—*Amputations in 1944 at Detroit Receiving Hospital*

Type	Number	Deaths	Percentage
Standard amputation	31	4	13
Refrigeration anesthesia	9	6	66
Total	40	10	25
Refrigeration anesthesia in 1947-1948 Standard amputation	23	2	8.7

tissue with possible extension of the gangrenous process by direct continuity of tissue. This concept has developed on the basis of sound experimental observations and is in agreement with known physiologic principles, as has been pointed out in a recent review of the subject by Ravdin and Johnston.[10] It is, therefore, not surprising that clinical experience with physiologic amputation by the tourniquet and refrigeration in suitable cases has been most gratifying.

8. Maxeiner, S. R.: The Temporary Tourniquet Amputation, Minnesota Med. **24**:491-492 (June) 1941.

9. Adolph, P. E.: Preoperative Measures Used in War Surgery in China with Special Reference to the Delimiting Tourniquet, Ann. Surg. **119**:246-252 (Feb.) 1944.

10. Ravdin, I. S., and Johnston, C. G.: Refrigeration in Surgery, Am. J. M. Sc. **209**:253-257 (Feb.) 1945.

CONCLUSIONS

Physiologic amputation by tourniquet and refrigeration is the method of choice in the management of the critically ill patient with a gangrenous extremity. After physiologic amputation, remarkable improvement in the patient's general condition may be anticipated. As a result, formal amputation, using spinal or general anesthesia, then may be undertaken above the cooled and ligated area with little risk. By amputation above the cooled and ligated area all the disadvantages of prolonged cooling of tissues are avoided.

Comparison of mortality figures among patients treated in this way with results obtained by other methods amply justifies the procedure. Sufficient experience now has been obtained to recommend this physiologic type of amputation for extensive clinical use in patients with moist gangrene of the extremities.

INTUSSUSCEPTION ASSOCIATED WITH ABERRANT PANCREATIC TISSUE

Report of a Case and Review of the Literature

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THE PURPOSE of this communication is to report an instance of intussusception in a 3½ year old boy in whom aberrant pancreatic tissue was found at the apex of the intussusceptum. A portion of the bowel containing the pancreatic tissue was found to be nonviable and was resected. A closed end to end anastomosis was done, and the patient made an uneventful recovery. Six cases found in the literature in which there were similar pathologic changes are summarized.

REPORT OF A CASE

T. W., a white boy aged 3½ years, was admitted to the Children's Surgical Service of Cook County Hospital on Feb. 10, 1942, because of nausea, vomiting and abdominal pain of sixty-six hours' duration. The child had been well until February 7 at 10 p. m., when he complained of nausea. Although he was restless and irritable, he slept until 3 a. m. the following morning, when he was awakened by crampy pain in the umbilical region which was of such severity that it caused the child to scream and grasp his abdomen. His pain decreased in severity, but he vomited about fifteen times throughout the day, usually immediately after taking small amounts of water. His bowels had not moved since the onset of the abdominal pain.

On February 9 crampy pain again was present and emesis occurred four or five times. The patient was given an enema of a half pint (250 cc.) of water. This increased his pain but did not cause any fecal material to be eliminated. A physician advised hospitalization. The child slept little during the night, and the pains continued. By noon the next day, February 10, the bowels had not moved. The patient was brought to the hospital. The inventory by systems revealed no additional information of importance.

The physical examination disclosed a well developed and well nourished white child. He was lying quietly in bed and appeared to be acutely ill. His rectal temperature was 100.4 F. The pulse rate was 130 per minute and the respiratory rate 28 per minute. Except for evidence of dehydration, the significant physical findings were confined to the abdomen. There were no scars or hernias. The abdomen was distended to a level 2 cm. above the xiphipubic line. Peristaltic waves were visible and more marked on the right. The bowel sounds were obstructive

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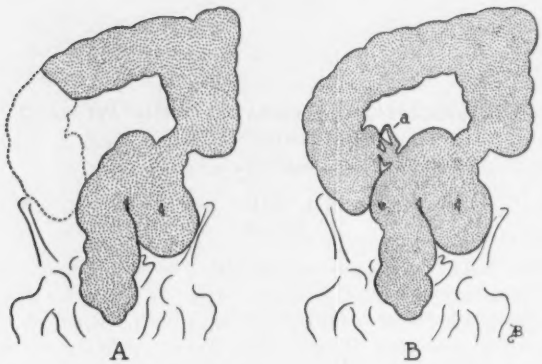

Fig. 1.—*A*, diagram showing outline of colon when barium was temporarily arrested just proximal to hepatic flexure, indicating an ileocolic intussusception. *B*, diagram showing outline of barium-filled colon and part of ileum after reduction of ileocolic intussusception. The "pitchfork" sign in the terminal portion of the ileum (*a*) indicates an unreduced ileoileal intussusception. This sign is the result of narrow columns of barium lying between the intussuscipiens and the intussusceptum and in the lumen of the latter.

Fig. 2.—Roentgenogram showing "pitchfork" sign in terminal portion of the ileum diagnostic of intussusception.

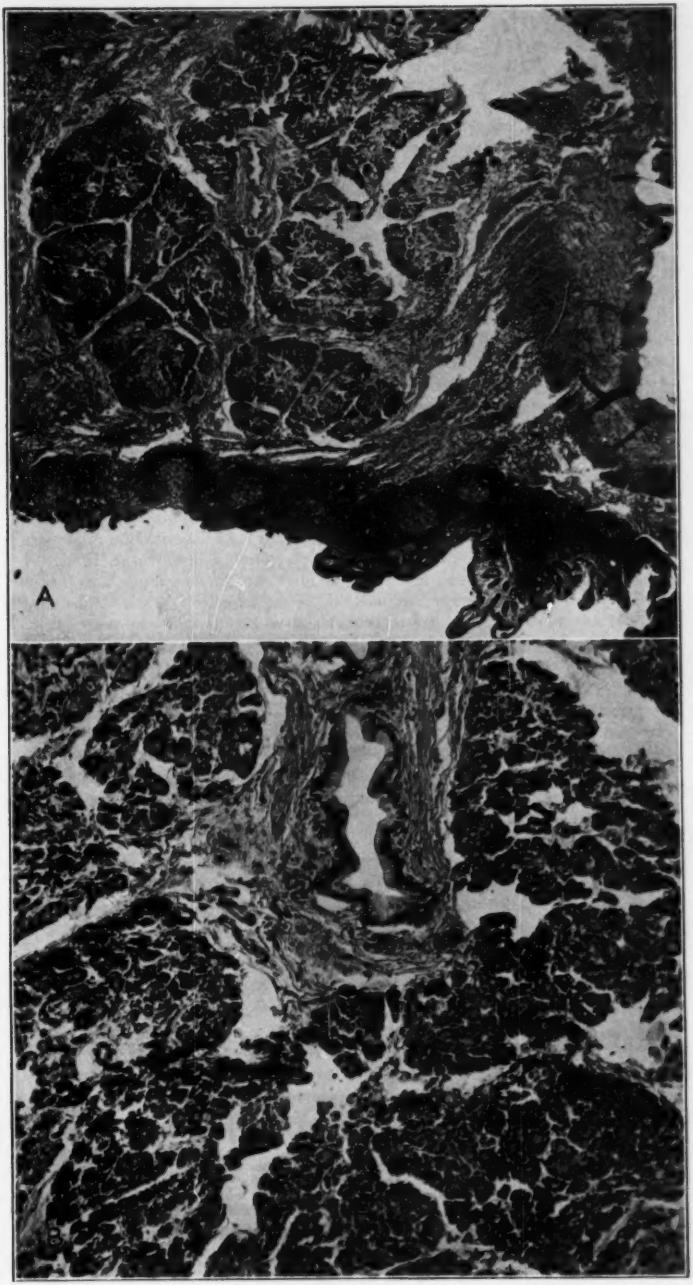

Fig. 3.—*A*, section of nodule shows it to be located in submucosal layer of wall of ileum. *B*, the high power magnification identifies the tissue in the nodule as pancreas.

in type.[1] Tenderness was diffuse but most marked over the lower right quadrant. Rectal examination did not disclose a mass. Although the diagnosis made in the admitting room had been acute appendicitis, the more detailed history and findings suggested the diagnosis of obstruction, probably due to intussusception. A plain roentgenogram of the abdomen disclosed dilated loops of small bowel.

Under the fluoroscope, barium solution was given by rectum and was seen to pass normally through the colon until it reached a point just proximal to the hepatic flexure. There the solution stopped, presenting a picture as shown in figure 1*A*. After approximately a minute, the column of barium slowly progressed toward the cecum, finally filling it normally and passing into the terminal portion of the ileum (fig. 1*B*). The ileum was regarded as being incompletely filled, which suggested the possibility of an ileoileal intussusception. This diagnosis was confirmed when the roentgenograms were examined (fig. 2). The "pitchfork" sign, diagnostic of intussusception, was present.

After the dehydration was corrected, morphine sulfate, 1/30 grain (2.1 mg.), and atropine sulfate, 1/300 grain (0.21 mg.), were given. Under general anesthesia the abdomen was opened through a right rectus incision, the rectus muscle being retracted laterally. When loops of moderately dilated small bowel were packed away an ileoileal intussusception was disclosed. This was reduced by "milking" the terminal portion of the ileum from below upward. As the reduction progressed, the intussusceptum was found to be the site of subserous hemorrhage, which discolored almost its entire length. At the head of the intussusceptum a nubbin of tissue about 1 cm. in diameter was seen on the antimesenteric border. This small mass appeared to lie in the intestinal wall and was covered by the seromuscular layer.

Because of the time which had elapsed since the onset of the intussusception, the discoloration, the extensive subserosal hemorrhage, the lack of pulsation and the presence of thrombi in the intestinal branches of the vessels supplying the area, resection of the involved ileum was done. A closed end to end anastomosis was performed, approximately 22 cm. of ileum being resected. After operation the patient received 250 cc. of plasma and 1,000 cc. of dextrose in saline solution. The postoperative temperature did not exceed 101 F. Gastric suction was discontinued after the second postoperative day. A spontaneous bowel movement occurred on the third postoperative day.

Microscopic examination of the nodule found at the head of the intussusception revealed pancreatic tissue, as shown in figure 3. The patient was dismissed on the twelfth postoperative day. Three weeks later he was readmitted for the treatment of a pyogenic infection of his right hand. The history disclosed that his appetite had been good, his bowels moved regularly every day and he had no abdominal complaints. He has remained well.

COMMENT

The theories of origin of aberrant pancreatic tissue have been summarized by Branch and Gross,[2] who pointed out that there is no explanation which has been found universally acceptable. Three general views concerning the origin may be presented as follows:

1. Vaughan, R. T., and Thorek, P.: Abdominal Auscultation, Am. J. Surg. **45**:230-234 (Aug.) 1939.

2. Branch, C. D., and Gross, R. E.: Aberrant Pancreatic Tissue in the Gastrointestinal Tract: A Report of Twenty-Four Cases, Arch. Surg. **31**:200-224 (Aug.) 1935.

The first concerns some deviation from the progression of events which terminates in the arrangement seen in the normal pancreas. The second theory holds that the occurrence of aberrant pancreatic tissue is an atavistic tendency and reproduces a condition seen in certain lower animals and fishes in which the pancreas is not an isolated organ but is diffusely scattered along the intestinal tract like other digestive glands. The third hypothesis is that of King and MacCallum,[3] who, after observing aberrant pancreatic tissue in the wall of the stomach four times, concluded that it arose from normal gastric mucosa under the influence of abnormal stimuli.

Aberrant pancreatic tissue occurs as yellow or white opaque lobulated masses, 1 to 4 cm. in their greatest dimension, and round or irregular in shape. In relation to the layers of the intestine, it is located in the submucosa in about 60 per cent of the cases, between the muscular layers in about 25 per cent and in the subserosa in only 4 per cent. According to a recent review,[4] it was found in the stomach, duodenum and jejunum in 69 per cent of the cases. The remaining sites included the ileum, intestinal diverticula and scattered areas, principally in the upper or middle portions of the abdomen.

Aberrant pancreatic tissue or pancreatic heterotopia is an uncommon condition as indicated by the recent review of Barbosa, Dockerty and Waugh,[4] who found only 430 cases reported up to March 1944. In routine autopsy material its incidence has been found to vary from 0.6 to 5.6 per cent. At the Mayo Clinic the incidence was 1.7 per cent at routine necropsies over a five year period. During the same period it was disclosed eighteen times at operation, or once in every 500 upper abdominal operations.

Obviously, as evidenced by the incidence at autopsy, many patients have no symptoms from aberrant pancreatic tissue. When clinical disturbances are present, they may be on the basis of direct mechanical obstruction caused by the size and location or indirect (and less common) obstruction caused by a disturbance in the local motility of the intestine, as in the cases of intussusception due to mural tumors.

A demonstrable cause of intussusception is an unusual finding. Gross and Ware[5] in their series of 610 cases of intussusception were able to demonstrate such causes as Meckel's diverticulum, intestinal

3. King, E. S. J., and MacCallum, P.: Pancreatic Tissue in the Wall of the Stomach, Arch. Surg. **28**:125-138 (Jan.) 1934.

4. Barbosa, J. J. de Castro; Dockerty, M. D., and Waugh, J. M.: Pancreatic Heterotopia: Review of the Literature and Report of Forty-One Authenticated Surgical Cases, of which Twenty-Five Were Clinically Significant, Surg., Gynec. & Obst. **82**:527-542 (May) 1946.

5. Gross, R. E., and Ware, [illegible]. F.: Intussusception in Childhood, New England J. Med. **239**:645-652 (Oct. 28) 1948.

polyps or enterocystomas in only 5.4 per cent. No instance of intussusception due to aberrant pancreatic tissue was reported in their large series. The recent entensive review of Barbosa, Dockerty and Waugh [4] concerning approximately 470 recorded cases does not list an instance of intussusception associated with aberrant pancreatic tissue as the sole abnormality. Harkins,[6] in a review of intussusception due to invaginated Meckel's diverticulum, stated: "Thus about forty-nine tumors of Meckel's diverticulum are on record, almost a third of which contain pancreatic tissue and over half of which have produced intussusception."

Branch and Gross,[2] in their review of 24 instances of aberrant pancreatic tissue, stated that cases of intussusception in which aberrant pancreatic tissue has acted as the leading point have been reported by Bize,[7] Brunner,[8] Hulst,[9] Taylor [10] and Benjamin.[11] However, the 2 cases reported by Bize concerned aberrant pancreatic tissue in diverticula in a boy and a girl aged 3 and 6 years respectively. Both died after operation for the relief of obstruction due to intussusception. The nodule of tissue at the apex of the diverticulum in each case was identified microscopically as pancreatic tissue. Brunner's case was that of a child aged 4 years whose intestinal obstruction was found to be due to intussusception caused by the invagination of a Meckel diverticulum which contained a mass of glandular tissue 25 mm. in diameter and identified microscopically as pancreatic. Resection of the involved area was done, and the patient recovered. The case reported by Hulst [9] was that of a 6 year old child in whom a diverticulum containing pancreatic tissue was found 10 cm. proximal to the ileocecal valve. Taylor's [10] patient (case 42) was a girl 4 years old with intussusception due to the invagination of a Meckel diverticulum which contained a nodule of pancreatic tissue. Recovery followed resection of the diverticulum.

Benjamin's [11] patient appears to be the only one in this list without an associated diverticulum. He was a 39 year old farmer with intus-

6. Harkins, H. N.: Intussusception Due to Invaginated Meckel's Diverticulum: Report of Two Cases with a Study of One Hundred Sixty Cases Collected from the Literature, Ann. Surg. **98**:1070-1095 (Dec.) 1933.

7. Bize: Etude anatomo-clinique des pancreas accessoires situes a l'extremite d'un diverticule intestinale, Rev. d'orthop. **15**:149-159 (March 1) 1904.

8. Brunner, C.: Ein Beitrag zur Chirurgie und pathologischen Anatomie der Darminvagination, Beitr. z. klin. Chir. **25**:344-363 (Nov.) 1899.

9. Hulst, J. P. L.: Ueber einem in einem Darmdivertikel gelagerten Pankreaskeim mit sekundarer Invagination, Centralbl. f. allg. Path. u. path. Anat. **20**: 12-15 (Jan.) 1909.

10. Taylor, A. L.: The Epithelial Heterotopias of the Alimentary Tract, J. Path. & Bact. **30**:415-449, 1927.

11. Benjamin, A. E.: Accessory Pancreas with Intussusception, Ann. Surg. **67**:293-298 (March) 1918.

susception in the upper portion of the jejunum. A tumor was found at the head of the intussusceptum and proved to be "an adenoma of accessory pancreas" on microscopic examination. It was intramural. The patient died on the fifth postoperative day.

A review of the literature since the report of Branch and Gross discloses 5 additional instances of intussusception associated with aberrant pancreatic tissue without a diverticulum. Azzolini [12] reported the case of a boy aged 7 years, who on admission was moribund owing to intestinal obstruction. At autopsy a "walnut-sized" oval tumor in the wall of the terminal portion of the ileum was found to be the cause of the intussusception, and the mass was identified microscopically as pancreatic tissue. The author emphasized the unusual nature of the case by calling attention to the previously reported instances of intussusception associated with aberrant pancreatic tissue in which there was also a diverticulum or a pedicle. The tumor in his patient was intramural. McLaughlin [13] described a case of irreducible intussusception in a child 8 months old. Resection of the terminal portion of the ileum and the ascending colon was done. The child recovered. The head of the intussusceptum was found to contain a tumor mass identified microscopically as pancreatic tissue and was located in the wall of the ileum.

Ripstein [14] reported an instance of an ileoileal intussusception in a girl aged 17 years who gave a history of recurrent attacks of colicky lower abdominal pain since childhood. A "walnut-sized" reddish gray tumor was found in the antimesenteric wall of the ileum 12 inches (30 cm.) from the ileocecal valve. A resection and an end to end anastomosis were done. Microscopic examination disclosed heterotopic pancreatic tissue in the submucosal layer of the ileum. The patient made an uneventful recovery. Bosworth and Stein [15] described a case of obstruction of the bowel due to intussusception in a 29 year old man. The intussusception was found to be irreducible and a resection of it was done, along with a primary end to end anastomosis. The patient made an uneventful recovery. Examination of the specimen disclosed a solid, firm, white mass in the wall of the ileum. It was covered with mucosa. The intussusception was 15 cm. proximal to the ileocecal junction. The tumor was 3 cm. in height and 2.5 cm. through the base. Micro-

12. Azzolini, O.: Invagination of Small Intestine Due to Accessory Pancreas: Case, Gazz. internaz. med.-chir. **45**:553-558 (Aug. 31) 1935.

13. McLaughlin, C. W., Jr.: Surgical Management of Irreducible Intussusception, Arch. Surg. **56**:48-55 (Jan.) 1948.

14. Ripstein, C. B.: Intussusception Due to Heterotopic Pancreas, Surgery **25**:76-77 (Jan.) 1949.

15. Bosworth, B. M., and Stein, H. D.: Intussusception in Adults: Report of a Case Due to Aberrant Pancreas, Am. J. Surg. **74**:801-804 (Dec.) 1947.

scopically the mass proved to be aberrant pancreatic tissue. There was no evidence of a diverticulum. Ravitch and McCune[16] list 8 instances (5.5 per cent) of intussusception due to demonstrable causes in a series of 144 patients treated at the Johns Hopkins Hospital from 1889 to 1947. Ectopic pancreatic tissue was the cause of an acute ileal intussusception in a 10 month old patient. The other lesions were polyps (5) and Meckel's diverticulum (3).

SUMMARY

A case of compound intussusception associated with aberrant pancreatic tissue in a 3½ year old boy is presented. Resection of the portion of ileum containing the mass of heterotopic tissue was followed by end to end anastomosis, with recovery. Pathologic study of the specimen disclosed the pancreatic tissue to be located in the submucosal layer of the wall of the ileum. This appears to be the seventh instance of intussusception with intramural aberrant pancreatic tissue as the only regional abnormality.

16. Ravitch, M. M., and McCune, R. M., Jr.: Reduction of Intussusception by Barium Enema, Ann. Surg. **128**:904-917 (Nov.) 1948.

MESENTERIC CYSTS

Report of Three Cases, in One of Which a Calcified Cyst Was Present

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THE PURPOSE of this paper is to present 3 cases of mesenteric cysts, 1 of which was a calcified cyst. In addition, certain data derived from a review of the literature will be presented in an attempt to add something to the knowledge of this relatively rare condition.

There have been many excellent articles written on this subject covering its various phases, and the reader is referred to a recent article by Vaughn, Lees and Henry, in which the previous literature has been summarized rather completely from the standpoint of history, etiology and classification and in which a case of calcified mesenteric cyst is reported. We have included only cases which were reported in sufficient detail to obtain certain pertinent facts and will present in tabular form the results in 197 cases reviewed plus the 3 cases reported in this paper, which make a total of 200 cases.

The incidence of mesenteric cyst has been variously estimated, and it is undoubtedly one of the rarest of all abdominal tumors. Classification according to age, sex, location of cyst, history and operative procedure used in the 200 cases reviewed is given in tabular form. From table 1 it would appear that the condition is more common in females, but unfortunately the sex of the patient was not stated in 24 of the case reports.

Table 2 indicates only the age of the patient at which symptoms presented themselves or at which the cyst was discovered accidentally.

The most common site of these cysts would seem to be in the mesentery of the small bowel although cysts have been reported in almost all possible locations. One might assume also that only cysts which are intimately associated with the intestinal tract are apt to give rise to difficulty while those of the omentum and retroperitoneum will not be discovered unless they attain a sufficiently large size or are found incidentally during other operative procedures.

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In 71 of the 200 cases histories were given in sufficient detail to make possible the observations in table 4. The exact character of the pain was not stated in a sufficient number of the case reports to obtain any definite statistics. The classical picture of mesenteric cyst is a

TABLE 1.—*Incidence According to Sex*

Sex	Number	%
Male	67	33.5
Female	109	54.5
Unknown	24	12

TABLE 2.—*Incidence According to Age*

Age, Yr.	Number	%
Less than 1	11	5.5
1 to 10	40	20.0
11 to 20	23	11.5
21 to 30	29	14.5
31 to 40	34	17.0
41 to 50	27	13.5
51 to 60	18	9.0
61 to 70	6	3.0
Unknown	12	6.0

TABLE 3.—*Location of Cysts*

Location	Number	%
Mesentery of small bowel	93	46.5
Mesentery of sigmoid	30	15.0
Mesocolon	22	11.0
Mesentery of cecum	16	8.0
Mesentery of descending colon	5	2.5
Mesentery of appendix	3	1.5
Omentum	4	2.0
Gastrohepatic mesentery	1	0.5
Duodenum	1	0.5
Retroperitoneum	10	5.0
Unknown	15	7.5

TABLE 4.—*History Obtained in 71 Cases*

Symptom or Finding	Number	%
Pain of some nature	58	81.5
Nausea and vomiting	32	45.0
Constipation	19	27.0
Diarrhea	4	5.5
Palpable mass	41	58.0

combination of low grade intestinal obstruction and the presence of a mass, usually freely movable. Pain was present in each of the 3 cases presented. In the first case there was a history of recurrent attacks of crampy abdominal pain. In the second, although there was pain of a crampy nature, it is impossible to state whether or not it was on the basis of the disease present in the gallbladder. In the third case there was a definite history of intermittent crampy pain associated with nausea.

In recent years the treatments of choice have been given as enucleation and resection, in that order. In some of the older articles marsupialization was listed as a favored form of therapy, but it was almost invariably accompanied with drainage over a prolonged period, from weeks to months. Undoubtedly, recent improvements in surgical technics and anesthesia have reduced the mortality rate of enucleation and resection so that it should probably be much lower than that found by this survey covering many years. This is particularly true of resection, which has a 15.9 per cent mortality rate in the series being presented.

REPORT OF CASES

CASE 1.—T. K., a white boy aged 7, was admitted to the hospital on Aug. 11, 1945.

History.—The patient complained of abdominal pain, which began when he awakened on the morning of admission. This pain was generalized and apparently crampy in nature and was accompanied with anorexia but no vomiting. Since the

TABLE 5.—*Procedure Used and Results Obtained*

Procedure	Total Cases	Recovery	Death	Result Unknown	Mortality, %
Enucleation	87	60	6	12	6.9
Resection	44	33	7	2	15.9
Marsupialization	23	21	1	1	4.4
Drainage	8	5	3	..	60.0
Aspiration	6	4	2	..	33.3
Laparotomy	27	11	7	9	....
Gastroenterostomy	1	..	1	..	....
Unknown	3	..	..	..	....
Autopsy	3	..	..	..	....

child had had previous similar attacks of pain, the mother was not particularly concerned and gave him a soap suds enema, which resulted in a liquid stool. There was no relief of pain, and it gradually became more severe in the lower part of the abdomen. During the remainder of the day the pain continued, and the child also had several liquid stools. There was one episode of vomiting following the ingestion of a mixture of soda, whisky and water. He was seen by Dr. Cucinotta at 4 p. m., who referred him to the hospital.

Past History.—The patient had had episodic attacks of generalized crampy abdominal pain with constipation and vomiting for a year and a half. These occurred at approximately monthly intervals and frequently seemed to be associated with an infection of the upper respiratory tract. In each case the pain would begin twenty minutes after a meal and would usually last for a day. However, one year before his admission, the child had an attack which lasted for three days, during which time he had obstinate constipation, anorexia, generalized abdominal pain and vomiting, the vomitus being greenish in appearance.

Physical Examination.—The patient seemed to be somewhat drowsy and was moderately toxic. The pharynx was inflamed. The remainder of the positive findings were limited to the abdomen, which appeared to be diffusely distended. Peristalsis was absent, and there was generalized muscle guarding. Generalized tenderness, which was slightly more marked in the right lower quadrant, and rebound tenderness were present. The abdomen was flat to percussion anteriorly

and more tympanitic in the flanks. No definite organs or masses were palpable. Rectal examination showed some tenderness on the right but no induration or masses. The temperature on the patient's admission to the hospital was 101 F.

Laboratory Findings.—The hemoglobin content was 12 Gm., erythrocytes 4,290,000, leukocytes 22,000, polymorphonuclear cells 81 per cent (filamentous forms 53, nonfilamentous forms, 28), lymphocytes 13 per cent, monocytes 2 per cent, eosinophils 3 per cent and basophils 1 per cent. The urine was normal except for a trace of albumin.

Operative Data.—A diagnosis of acute appendicitis was made in view of the leukocytosis and the localizing signs in the right lower quadrant. The child was taken to the operating room at 11 p.m. Under spinal anesthesia, a 2 inch (5 cm.) transverse incision was made centering over McBurney's point. The external oblique, internal oblique and transversalis muscles were split in the line of their fibers, and the peritoneum was incised. Immediately there was visualized a large fluctuant mass. In order to obtain better exposure, the incision was enlarged, and it was found that this mass was a large mesenteric cyst arising from the mesentery of the ileum. It was hourglass in appearance, and one wall composed about 6 cm. of the serosa of the small intestine. The cyst ballooned out on both sides of the mesentery and extended down it for about 6 cm. to about the level of the transverse arcade, proximal to the bowel. Each of the lateral portions was approximately 6 inches (15 cm.) in diameter, and these were connected by a narrow channel through the mesentery, which just admitted the tip of the index finger. The cyst was not tense, which explains why it could not be felt through the abdominal wall. Since the incision was not adequate for removal of the cyst and resection of the attached portion of bowel and since there had been no perforation, it was decided merely to decompress it. The contents proved to be chylous in appearance. The appendix was then found where it had been lying beneath the cyst, and it proved to be suppurative. An appendectomy was done. The patient made an uneventful recovery, and he was discharged on the sixth postoperative day.

The patient was given a month for convalescence and then readmitted on Sept. 18, 1945. He had been completely symptom free during the interval. On his second admission his urine was completely normal and his blood count was normal, with a hemoglobin content of 12.6 Gm., erythrocytes 4,870,000 and leukocytes 7,000, with a normal differential count. The total serum protein content was 8.5 Gm. per hundred cubic centimeters. He was prepared for six days with succinylsulfathiazole, 1 Gm. every four hours. On September 26, with the patient under spinal anesthesia, a 10 cm. paraumbilical incision was made on the left side. The mesenteric cyst and adjacent bowel were delivered into the incision, and the mesentery containing the cyst and the adjacent small bowel were resected. A modified closed anastomosis was done.

For two days postoperatively the patient was given intravenous infusions of amigen® and was kept on continuous gastric suction. On the third postoperative day the Levin tube was clamped and sips of water were given by mouth, and the following day the tube was removed. In addition, he was given ascorbic acid and vitamin B complex parenterally. By the eighth postoperative day he was on a soft diet, and he was discharged on the tenth day. For two days postoperatively the temperature rose to 99.6 F. (rectal) and then remained normal.

The pathologic report was "a simple cyst of the mesentery." The patient has remained entirely symptom free for over three years.

Comment.—This case is unique among those reported in the literature in that there was acute appendicitis associated with a mesenteric cyst. Although the acute clinical picture was probably due entirely to the appendicitis, the cyst had caused chronic symptoms of partial obstruction of the small bowel. Because the cyst was not tense, a mass was not felt on abdominal examination. However, had there been no tenderness, perhaps a mass might have been palpated.

Cysts of this type are often diagnosed by chance.

CASE 2.—M. W., a white woman aged 28, was admitted to the hospital on June 18, 1945.

History.—The patient stated that she was completely well until December 1944, when she had her first attack of pain in the right upper quadrant. Then she had six to eight such attacks. The pain would usually radiate to the back. She had no qualitative or quantitative dyspepsia. An attack of pain began suddenly about ten hours before her admission. Since the onset she had had nausea and vomiting.

Past History.—The patient had been severely constipated for three years. Also she had undergone appendectomy thirteen years before her admission. Approximately one month before her admission she was hospitalized, and at that time a mass was palpated in the left lower quadrant of the abdomen. On pelvic examination, this seemed to be an ovarian cyst the size of an orange. An abdominal exploration was done, and a cyst in the mesentery of the sigmoid was found. An attempt was made to enucleate this cyst, but it was ruptured. There were also noted several smaller cysts in the sigmoid mesentery.

Physical Examination.—The patient was a fairly well nourished white woman who apparently had a moderate amount of discomfort. The only positive finding on examination was tenderness in the right upper quadrant. There were no masses at this time, and nothing abnormal was noted on pelvic examination.

Laboratory Findings.—The blood count on admission showed a hemoglobin content of 12.1 Gm. and 3,790,000 erythrocytes. The leukocytes numbered 10,500, with 78 per cent polymorphonuclear cells (filamentous forms, 48, and nonfilamentous forms, 30), 19 per cent lymphocytes, 2 per cent monocytes and 1 per cent eosinophils. Urinalysis showed a specific gravity of 1.027 and a negative reaction to the tests for albumin and occult blood. A positive reaction for sugar was obtained, but the blood sugar was normal.

Operative Data.—On June 20, 1945, the patient was taken to the operating room and spinal anesthesia produced; the abdomen was entered through a vertical right upper rectus incision. The gallbladder was found to be somewhat thickened and contained many small, faceted stones. The cystic duct was dilated, and the common duct was slightly enlarged. Exploration of the common duct revealed at least four small stones. A cholecystectomy was done. In addition, the sigmoid was delivered into the wound and several cysts were found in its mesentery. These were multilocular, with thin walls. The largest one contained bloody fluid. All the cysts were enucleated. The abdomen was closed, a sump drain being left in the gallbladder bed and a T tube in the common duct.

Pathologic examination revealed the following histologic changes: The cyst wall was composed of fibrofatty tissue and was infiltrated with leukocytes. There was no definite cell lining. The diagnosis was mesenteric cyst. Microscopic examination of the gallbladder showed chronic cholecystitis.

After the operation the patient made an uneventful recovery, and she was discharged from the hospital on her ninth postoperative day in good condition. We attempted to obtain follow-up data on this patient but have been unable to do so.

Comment.—In this case the finding of mesenteric cysts was purely incidental. The symptoms were those of disease of the biliary tract. Cysts such as these usually, if not always, gradually increase in size and produce pressure symptoms later. They should be removed.

CASE 3.—B. P., a white woman aged 44, was admitted to the hospital on May 14, 1948.

History.—The patient had been having nausea and a dull aching pain in the right side of the abdomen for several months. The pain had not been constant and never too severe. There had been no other disturbance referable to the gastrointestinal tract.

Physical Examination.—The patient was a well developed woman in no apparent distress. The positive findings were limited to the abdomen. There was a suprapubic midline scar, and a freely movable firm mass approximately 5 by 5 cm. was palpated in the general area below and to the left of the umbilicus. This mass was so freely movable that it was difficult to state its definite position. It was regular in outline, firm and not tender.

Laboratory Studies.—The blood count on admission showed a hemoglobin content of 13.8 Gm. and 4,790,000 erythrocytes. The leukocytes numbered 7,200, with a differential count as follows: polymorphonuclear cells, 44 per cent; lymphocytes, 41 per cent; monocytes, 5 per cent, and eosinophils, 9 per cent. The urinalysis showed a specific gravity of 1.021 and a negative reaction for albumin, sugar and occult blood. Microscopic study of the urinary sediment showed only 7 to 9 leukocytes per high power field.

The roentgenogram of the chest showed a normal condition. Roentgenograms of the abdomen demonstrated some calcification of the mass.

Operative Data.—The patient was taken to the operating room on May 18, 1948, and spinal anesthesia produced; the old midline scar was reopened and the abdomen explored. There was found a hard, circumscribed tumor on the anterior surface of the mesentery of the ileum, adjacent to the mesenteric attachment of the bowel. The mass was carefully dissected free, and then there was noticed some venous engorgement of that portion of small bowel. Since there was considerable question of the adequacy of the blood supply, this 12 cm. segment of bowel was resected and an open end to end anastomosis done, two rows of chromic surgical gut being used for the mucosal and serosal layers. Five grams of sulfanilamide, 100,000 units of penicillin and 1 Gm. of streptomycin were instilled in the abdomen, and the wound was closed without drainage.

When the tumor mass was sectioned, it was found to be a cystic structure 4 cm. in diameter. The wall was 0.5 cm. in thickness and was partially calcified. The cyst contained a yellow putty-like material. On microscopic section the wall was found to be made up of broad bands of hyalinized collagenous material, which in some areas contained specks of calcium and collections of lymphocytes, the latter suggesting that the process may have arisen in a lymph node. The diagnosis was calcified cyst of the mesentery.

After the operation the patient made an uneventful recovery. The temperature rose to 100.8 F. on the first postoperative day but subsided to normal by the third day. She was discharged from the hospital on the ninth day. Two months after her discharge a roentgenogram showed an entirely normal gastrointestinal tract. The patient has remained symptom free during the seven months since operation.

Comment.—In this case the symptoms presented were undoubtedly due to the presence of the mesenteric cyst. They probably represent the most typical clinical picture of mesenteric cyst. However, a calcified cyst is extremely rare.

COMMENT

When a rounded circumscribed mass is palpated or is incidentally seen on a roentgenogram because of calcification in its walls, the possibility of mesenteric cyst must be considered. The diagnosis is especially likely when there are symptoms suggesting a low grade intestinal obstruction. Because of its location, a mesenteric cyst will often be so freely movable as to vary markedly in location from the time of one examination to another. Since the diagnosis cannot be made positively without an operation, exploration is imperative to rule out other, more serious, tumors. A mesenteric cyst is more or less innocuous in itself, but a positive diagnosis cannot be made without abdominal exploration. Since the location of the cyst in the mesentery is often close to the bowel, gradual increase in size may produce increasing intestinal obstruction. The operation can usually be done as an elective procedure, but the cyst should be removed.

Before surgical intervention the bowel should be adequately prepared so that if enucleation of the cyst jeopardizes blood supply to the bowel a resection can be done with relative safety.

SUMMARY

Three cases of mesenteric cyst are presented. In 1 the cyst was definitely producing symptoms, in 1 it was the questionable cause of symptoms and in the other it was picked up incidentally.

BIBLIOGRAPHY

Benedict, A. L.: Bibliography of Chylous Cysts of the Mesentery, Surg., Gynec. & Obst. **16**:606, 1913.

Berger, L., and Rothenberg, R. E.: Cysts of the Omentum, Mesentery and Retroperitoneum: Clinical Study of Eighteen Cases, Surgery **5**:522, 1939.

Block, F. B.: Chylous Mesenteric Cyst, Ann. Surg. **128**:158, 1948.

Carter, R. M.: Cysts of the Mesentery, Surg., Gynec. & Obst. **33**:544, 1921.

Collins, A. N., and Berdez, G. L.: Chyle Cysts of the Mesentery, Arch. Surg. **28**:335 (Feb.) 1934.

Dutton, F. K.: Report of Case of Ruptured Chylous Mesenteric Cyst, New England J. Med. **203**:1032, 1930.

Eliason, E. L., and North, J. P.: Perforated Chylous Cyst of the Mesentery, Ann. Surg. **101**:1452, 1935.

Flynn, C. W.: Mesenteric Cysts, with Report of Case of Cystic Lymphangioma, Ann. Surg. **91**:505, 1930.

Gale, J. W., and Keeley, J. L.: Mesenteric Cysts Causing Intestinal Obstruction, Am. J. Surg. **40**:647, 1938.

Gaston, E. A.: Cystodenoma of the Ovary Incorporated Between the Leaves of the Mesosigmoid, Surgery **6**:389, 1939.

Goldberg, S.; Widerman, A. H., and Friedman, P. S.: Congenital Mesenteric Cyst Associated with Failure of Rotation of the Intestinal Tract: Report of Case, Arch. Pediat. **57**:499, 1940.

Guthrie, R. F., and Wakefield, E. G.: Mesenteric Cysts, Proc. Staff Meet., Mayo Clin. **18**:52, 1943.

Hastings, J. P.: Mesenteric Cyst, Brit. M. J. **1**:947, 1934.

Jackman, W. A., and Mayston, E. A.: Cysts of the Mesentery, Brit. M. J. **2**:1079, 1936.

Jewesbury, R. C.: Lymphatic Cyst of the Mesentery and Volvulus in a Child, Lancet **1**:1170, 1937.

Judd, E. S., and Crisp, N. W.: Primary Tumors of the Mesentery, Proc. Staff Meet., Mayo Clin. **7**:555, 1932.

Judd, E. S., and Heimdal, O. C.: Mesenteric Cysts, Surg. Clin. North America **12**:849, 1932.

Kross, I.: Mesenteric Cysts, Rev. Gastroenterol. **9**:281, 1942.

Larkin, F. L.: Mesenteric Cysts, Pennsylvania M. J. **43**:1446, 1940.

Loeb, M. J.: Mesenteric Cysts: Review of Literature, Genesis and Classification, New York State J. Med. **41**:1564, 1941.

Lubitz, J. M., and Flynn, R. W.: Chylangioma Cavernosum Mesenterii, Surgery **18**:772, 1945.

Millar, R. E., and Robertson, G.: Enterocystoma, Brit. J. Surg. **17**:373, 1929-1930.

Miller, L. A.: Rarity of Congenital Mesenteric Cyst, Am. J. Dis. Child. **50**:1196, 1935.

Muir, J. B. G.: Mesenteric Cyst Causing Attacks of Subacute Obstruction in a Child, Lancet **1**:742, 1935.

Nordland, M., and Larson, L. M.: Mesenteric Cyst, Ann. Surg. **101**:1289, 1935.

Parsons, Eugene O.: True Proliferating Cystic Lymphangioma of the Mesentery, Ann. Surg. **103**:595, 1936.

Paul, M.: Mesenteric Cysts, Brit. J. Surg. **35**:308, 1948.

Peterson, E. W.: Adenocarcinoma in a Cyst of the Transverse Mesocolon, Ann. Surg. **97**:782, 1933.

Cysts of the Mesentery, Ann. Surg. **112**:80, 1940.

Mesenteric and Omental Cysts, Ann. Surg. **96**:340, 1932.

Phelan, G. W.: Mesenteric Cyst, Am. J. Surg. **22**:321, 1933.

Rea, C. E.: Enterogenous Cyst: Observation of Unusual Physical Sign, Ann. Surg. **112**:300, 1940.

Riggall, F., and Riggall, C.: Mesenteric Cyst, Brit. M. J. **1**:345, 1940.

Roller, C. S.: Mesenteric Cysts: Brief Discussion and Report of Three Cases, Surg., Gynec. & Obst. **60**:1128, 1935.

Schunke, G. B., and Waugh, J. M.: Mesenteric Cyst: Report of a Case, Proc. Staff Meet., Mayo Clin. **16**:676, 1941.

Slocum, M. A.: Surgical Treatment of Chylous Mesenteric Cyst by Marsupialization, Am. J. Surg. **41**:464, 1938.

Stewart, J. and Mallory, T. B.: Case Report: Mesenteric Cyst, New England J. Med. **213**:1251, 1935.

Vaughn, A. M.; Lees, W. M., and Henry, J. W.: Mesenteric Cysts, Surgery **23**:306, 1948.

Warfield, J. Ogle, Jr.: Study of Mesenteric Cysts with Report of Two Recent Cases, Ann. Surg. **96**:329, 1932.

HISTOLOGIC LOCALIZATION OF ABSORBED RADIOACTIVE IODINE IN SOME HUMAN THYROID DISEASES

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IN 1940 Hamilton, Soley and Eichorn [1] described a method of localizing administered radioactive iodine in the human thyroid. Patients were given an oral tracer dose of radioactive iodine prior to operation. Histologic sections were made of the excised portion of the gland and the secretions placed in contact with unexposed photographic film. Areas of uptake of radioactive iodine in the section produced a blackening on the film. With this technic, these authors found the greatest uptake of iodine in areas of hyperplasia. Of great interest was their observation that the carcinomatous tissue in two thyroid studies showed no uptake. Since their publication, there have been a few reports of thyroid carcinomas showing appreciable uptake of iodine.

These authors also noted that the concentration of radioactive iodine was great in the more cellular regions of the thyroid and did not show any predilection for the colloid. LeBlond [2] in 1942, 1943 [3] and 1946 [4] published results showing that in both the experimental animal and in the human being radioactive iodine is stored mainly in the colloid. LeBlond also observed that glands stimulated with thyrotropic hormone

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From the divisions of medicine, radiology and pathology of the University of California Medical School, San Francisco.

1. Hamilton, J. G.; Soley, M. H., and Eichorn, K. B.: Deposition of Radioactive Iodine in Human Thyroid Tissue, Univ. California Publ., Pharmacol. **1**:339-368 (Nov.) 1940.

2. LeBlond, C. P.: Localization of Newly Administered Iodine in Thyroid Gland as Indicated by Radio-Iodine, J. Anat. **77**:149-152 (Jan.) 1943.

3. LeBlond, C. P.: Behavior of Radio-Iodine in Resting and Stimulated Thyroids, Anat. Rec. **88**:285-290 (March) 1944.

4. LeBlond, C. P.; Fertman, M. B.; Pukkel, I. D., and Curtis, G. M.: Radio-Iodine Autography in Studies of Human Goitrous Thyroid Glands, Arch. Path. **41**:510-515 (May) 1946.

stored more radioactive iodine than normal glands. The latter observation has been confirmed by Keating and others.[5] Keating and his associates further noted that in cases of thyroid hyperplasia produced by administration of thyrotropic hormone the uptake of radioactive iodine could be increased over that of normal glands.

MATERIAL AND METHODS

The present study was undertaken to determine the localization of I^{131} in the thyroid glands of patients with various thyroid diseases. Thirty-five patients were studied. Three had thyrotoxicosis with diffuse thyroid enlargement. Thirteen had nodular goiters; two of these glands contained benign neoplastic nodules, and the remainder were involutionary nodular glands. Four patients had thyroiditis, and 15 of the patients had thyroid carcinoma.

An oral tracer dose of I^{131} (the eight day isotope), free of carrier iodine, was given one to five days before operation. Except in a few cases of carcinoma, the dose was 250 microcuries. Twenty-four hours after ingestion of the iodine, the total uptake of the dose in thyroid, in terms of the percentage of the administered dose, was measured by the Geiger counter. If there was a possibility of thyroid metastasis, the whole body was surveyed with a Geiger counter in an attempt to locate it. At this time the percentage uptake was nearly maximal. The average patient in this series in the enthyroid state fixed about 20 per cent of the administered dose, or 50 microcuries, in their gland. The average weight of the gland was about 25 Gm. Several normal patients received the described amount of radioiodine and showed no demonstrable clinical or laboratory evidence of thyroid depression. The matter of dosage of radioactive iodine is discussed in the papers of Nickson [6] and Seidlin and others.[7] The weight of the iodine administered is very small, approximately 10^{-11} Gm., so that no metabolic change due to an increment of iodine might be anticipated. The tissues from the thyroid or from areas of metastasis were obtained immediately after surgical excision and their content of radioiodine measured. Whenever possible, the uptake of weighed amounts of carcinomatous tissue was determined separately from that of surrounding normal tissue. The carcinomatous tissues were then fixed in formaldehyde, and paraffin sections were made

5. Keating, F. R., Jr.; Rawson, R. W.; Peacock, W., and Evans, R. D.: Collection and Loss of Radioactive Iodine Compared with Anatomic Changes Induced in Thyroid of Chick by Injection of Thyrotropic Hormone, Endocrinology **36**:137-148 (Feb.) 1945.

6. Nickson, J. J.: Dosimetric and Protective Considerations for Radioactive Iodine, J. Clin. Endocrinol. **8**:721-731 (Sept.) 1948.

7. Seidlin, S. M.; Marinelli, L. D., and Oshry, E.: Radioactive Iodine Therapy: Effect on Functioning Metastases of Adenocarcinoma of the Thyroid, J. A. M. A. **132**:838-847 (Dec.) 1946.

in the usual manner. The paraffin was extracted with xylol. The sections were processed within twenty-four hours. In the darkroom a strip of unexposed film was placed emulsion side to the section and several glass slides were placed on the outer sides of the film and the section. A few rubber bands placed around the bundle of slides held the film firmly against the section. The film and the section were then wrapped in light-tight paper and left in contact until the film was properly exposed by the radiation from the fixed radioactive iodine. Several such glass film packages were made from each gland, and the first film was developed three days later. Usually this was adequate, but if the exposure was insufficient other sections were developed at a later date. With our technic the longest useful exposure was obtained in about eight days. By that time the decay of the iodine had proceeded to such an extent that further blackening of the film could not be demonstrated. After exposure the sections were stained with hematoxylin and eosin. The areas of blackening of the film could then be correlated with the corresponding area on that section. Although a variety of films were tried, dental film was used because of its convenience, adequate sensitivity to beta radiation and adequate resolution. The films were then processed in the usual manner and mounted on glass slides.

RESULTS

1. *Nodular Glands.*—Most of the nodules studied were from thyroid glands containing involutionary nodules. The microscopic appearance of these nodules varied from frank hyperplasia to marked involution. In considering involutionary nodules it was found that the greater the hyperplasia the greater the uptake of iodine, as measured by the Geiger counter and as determined by the degree of blackening on the radioautograph for the same administered dose and time of exposure. Correspondingly, the total uptake of the involuted gland as measured on the Geiger counter might be in the region of 20 per cent of the administered dose while the hyperplastic gland would show a much greater total uptake, ranging from 40 to 60 per cent of given iodine. Figure 1 illustrates a fairly diffuse distribution of iodine in an involutionary nodule. Figure 2 shows that the iodine appears mostly in the lining cells of the acini rather than in the colloid. This is in part a function of the amount of time between administration of the iodine and operation. With intervals of three days or less from ingestion to operation, most of the iodine appears in the cells. With longer intervals, appreciable quantities appear in the colloid.

An interesting impression gained in the study of the nodules is that those that have dense or thick capsules often show less uptake than other nodules of similar size and histologic appearance taken from the same gland but without the limiting capsule.

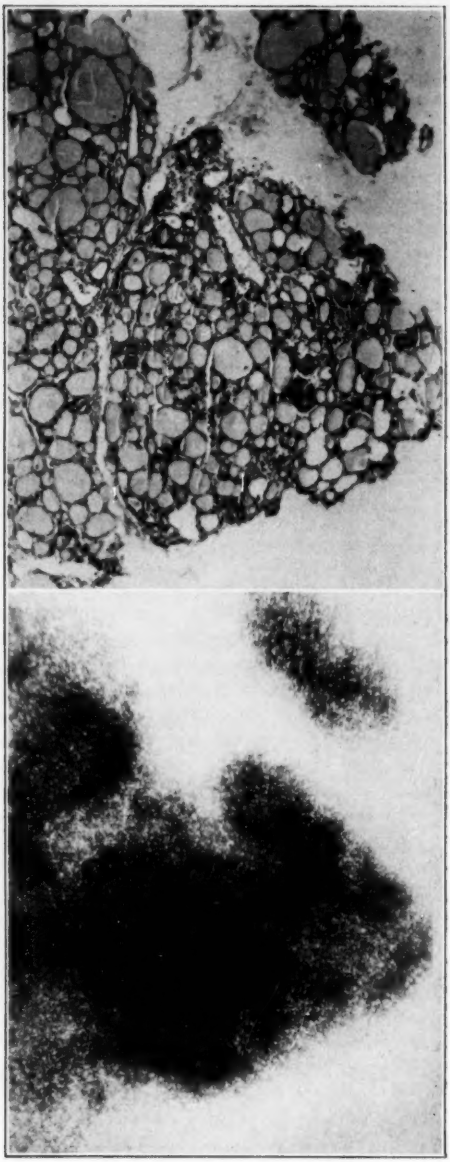

Fig. 1.—Involutionary nodule.

Figure 3 shows an adenoma of the simple type from a nontoxic nodular goiter. The patient had received no iodine except the tracer dose. In spite of the hyperplastic appearance, it is apparent from the

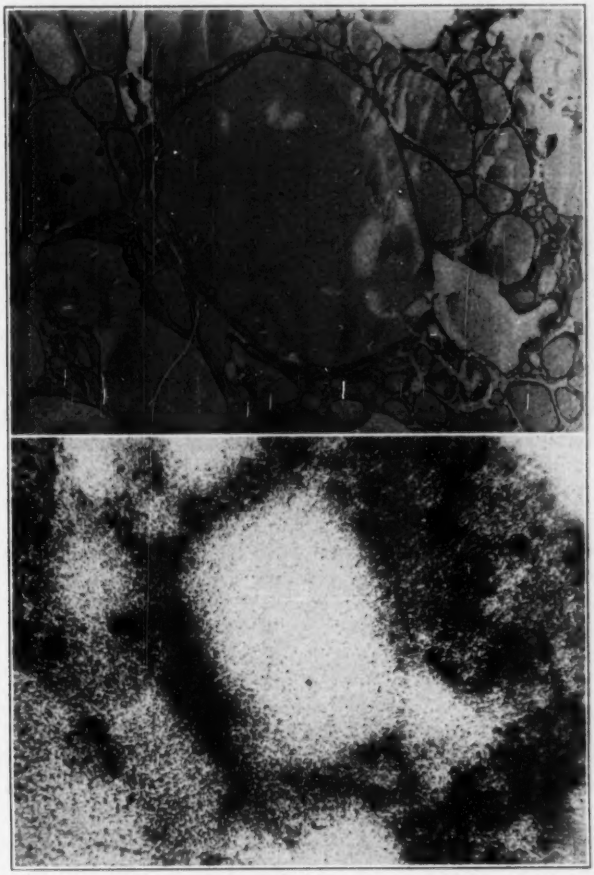

Fig. 2.—Involutionary nodule showing deposition of iodine in the acinar epithelium and not in the colloid.

accompanying radioautograph that there is little uptake. This gland had in it some nodules which were definitely involutionary, and these had a characteristically good uptake. In another patient a low uptake was observed in a fetal adenoma; the remaining normal thyroid showed a

good uptake. In this connection, Dobyns and Lennon have published a report [8] in which there is radioautograph from an embryonal adenoma showing no uptake in the adenoma.

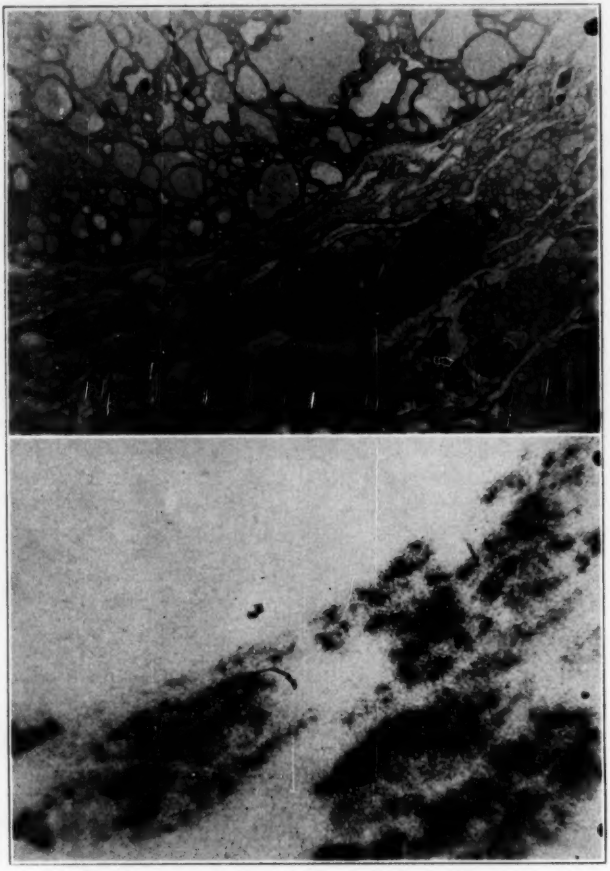

Fig. 3.—The left half of the section is adenoma and the right half normal thyroid. A failure of uptake in the neoplastic adenoma is demonstrated.

8. Dobyns, B., and Lennon, B.: A Study of the Histopathology and Physiologic Function of Thyroid Tumors Using Radioactive Iodine and Radioautography, J. Clin. Endocrinol. **8**:732-748 (Sept.) 1948.

2. *Toxic Diffuse Goiter.*—The thyroids of 3 patients with toxic goiters were examined. These patients had received strong iodine solution before operation, and the histologic appearance of the gland was that of involuting hyperplasia. These glands had a low uptake demonstrable by both the Geiger count and the radioautograph method. This can be explained by the preoperative saturation with iodine. Previous to administration of strong solution of iodine the total iodine uptake had ranged from 40 to 60 per cent in these patients, and concomitant with the drop in clinical toxicity, the percentage uptake of administered radioactive iodine fell to levels below 20 per cent. Glands from patients who received strong iodine solution and who had had diffuse thyrotoxicosis show a low uptake of I^{131} evenly distributed throughout when the radioautograph is studied.

3. *Thyroiditis.*—Four patients with thyroiditis were studied with the combined radioautograph and total glandular uptake method. In all cases the total uptake in Geiger counts was less than 9 per cent of the total dose and the radioautographs showed a spotty uptake, largely confined to whatever groups of normal-appearing cells remained. The large areas of lymphocytic infiltration and the areas of disorganized acinar structure had no demonstrable uptake. Figure 4 illustrates the spotty, low uptake.

4. *Thyroid Carcinoma.*—In the 15 cases of thyroid carcinoma both the primary carcinoma and the area of regional metastasis were available for study in 6 cases, the primary carcinoma in 5 cases and tissue from the area of metastasis only in 4 cases. There was one anaplastic, one Hürthle cell and one papillary carcinoma, and there were two adenocarcinomas. The remainder were classed as papillary adenocarcinomas. Except for one striking exception, none of the fifteen took up iodine.

Figure 5 illustrates the typical picture of a gland with papillary adenocarcinoma. The high uptake of radioiodine in the remaining normal cells can be clearly seen, while the lack of iodine fixation is evident in the fibrous tissue reaction and the growing papillary adenocarcinoma. Though the total uptake of the extirpated gland was 20 per cent, it was almost entirely confined to the normal, noninvaded thyroid. The papillary adenocarcinoma had no uptake. Comparison of the radioautograph and the section shows a few tiny spots of uptake in areas that are apparently all carcinoma. However, careful study shows these areas to be correlated with tiny isolated islands of normal gland, the probable remnants of the invaded gland, instead of with the carcinoma itself. This same situation of apparent minute tumor uptake was seen in other carcinomas, and a similar explanation holds.

The one instance of a substantial uptake was in an area of lymph node metastasis in the neck. The patient was a 27 year old white man.

The diagnosis of thyroid carcinoma with pulmonary metastasis had been made and confirmed seventeen years previously. In the intervening years he had remained essentially asymptomatic except for moderate pressure symptoms from slowly enlarging cervical glands. A series of

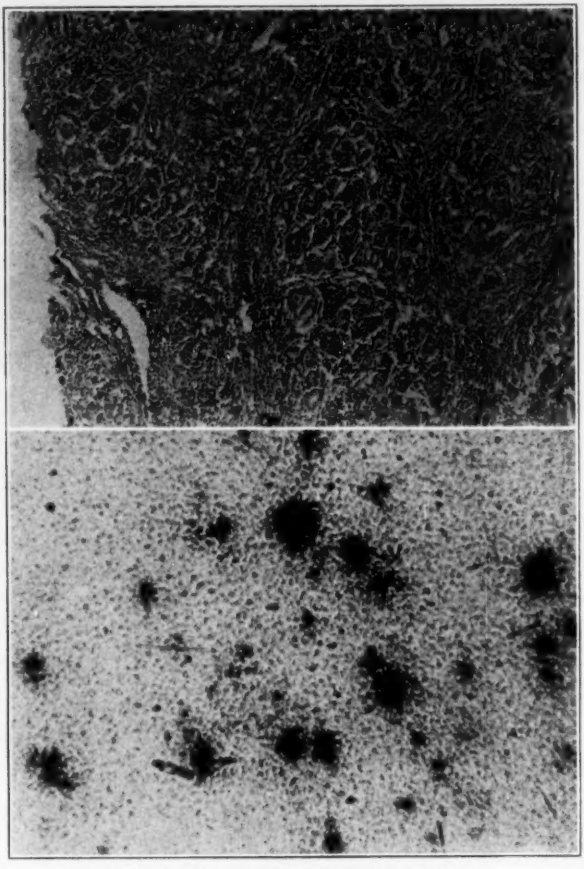

Fig. 4.—Spotty, small uptake of thyroiditis.

roentgenologic studies from the time of the original diagnosis to the present had shown only slight increase in the area of pulmonary metastasis. The first test dose of 2 millicuries in this patient demonstrated an uptake of 16 per cent, and a second test study two months

later showed an uptake of 20 per cent. Several years previously, this patient had undergone total thyroidectomy. Therefore, this uptake was due to functioning metastatic tissue. Clinically the patient did not have hypothyroidism. Presumably his thyroid hormone was supplied by

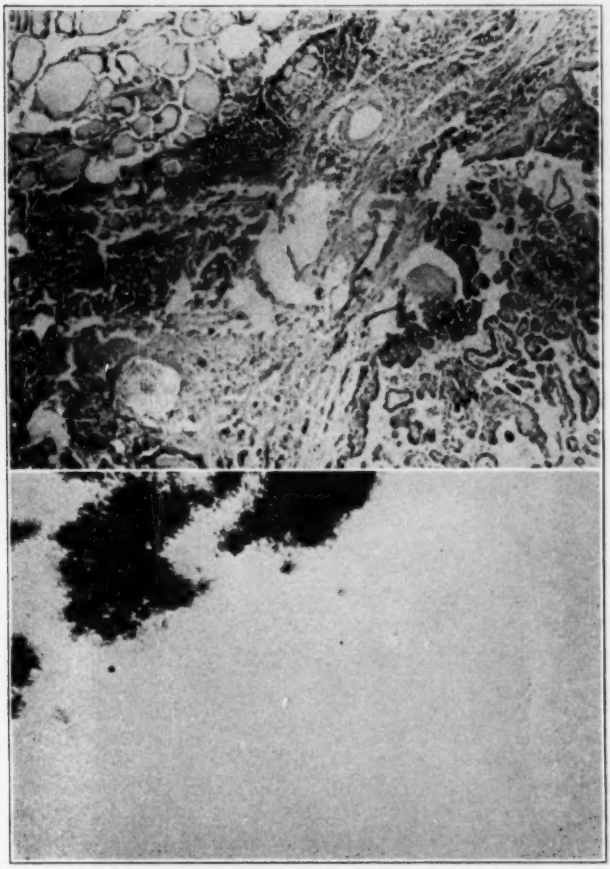

Fig. 5.—The remaining normal tissue is in the upper right corner and the bulk of the carcinoma tissue in the lower right corner. The failure of uptake in carcinoma tissue is demonstrated.

the area of carcinoma metastasis. Study of the chest with a Geiger counter indicated a significant uptake in the area of pulmonary metastasis. After a test dose a biopsy of a cervical lymph node was carried

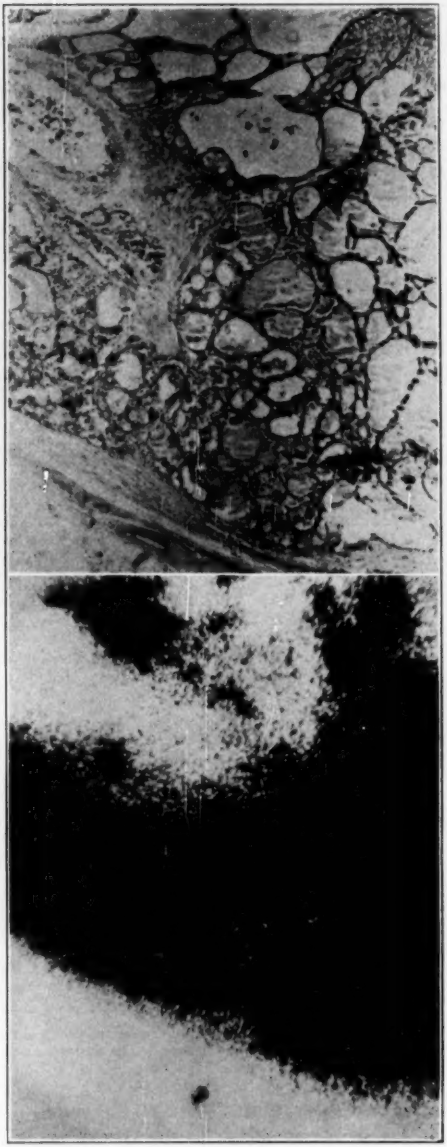

Fig. 6.—Appreciable uptake in a lymph node by thyroid carcinoma.

out, and it was shown to contain 4 microcuries of radioactive iodine per gram. With the use of the method already outlined, this would indicate that with a therapeutic dose of 75 millicuries about 22,500 equivalent roentgens would be delivered to the metastatic thyroid tissue, assuming that there is total decay of the I^{131} in the tissue. Histologic sections showed a well differentiated papillary adenocarcinoma with definite acinar structures and well staining colloid which had almost entirely replaced the invaded lymph gland. The radioautograph and section from the node in figure 6 show a demonstrable uptake throughout most of the carcinoma. However, some areas are less acinar, more papillary and irregular, and these have a greatly lessened uptake compared with the more acinar areas. An attempt was made to treat the patient with

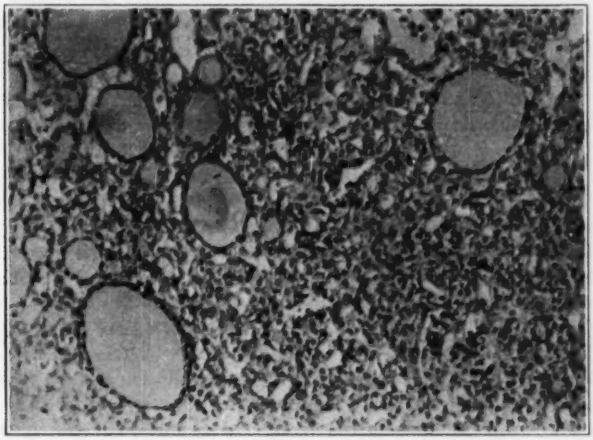

Fig. 7.—Section of a scalp metastasis from a thyroid carcinoma showing well formed acini. This area of metastasis had no demonstrable uptake of radioactive iodine.

a therapeutic dose of 75 millicuries; however, the inference one draws from the radioautographic study is that while this will probably destroy the largest portion of the metastatic tissue, certain areas may not take up enough for adequate radiation and will remain for further growth.

In several of the carcinomas, minute uptakes of radioactive iodine could be demonstrated. However, these uptakes were too small to consider therapy with isotopic iodine since the radiation tolerance of the kidneys would probably be exceeded if a dosage of roentgen rays sufficient for the purpose were delivered. This follows because at least three quarters of the radioactive iodine would probably be excreted via the kidneys.

Figure 7 shows a metastatic lesion of the scalp in which there is definite formation of acini containing colloid and in which no iodine uptake could be demonstrated. This illustrates the fact that even though the carcinoma may have some of the appearances of functional thyroid tissue, its behavior, as judged by iodine uptake, shows that it does not have the iodine-collecting power of normal thyroid.

COMMENT

With regard to the differences of behavior of iodine uptake in hyperplastic and involuted thyroids, this paper merely offers further confirmation of the already well described fact that hyperplastic tissue takes up a good deal more iodine than involuted tissue. As would be expected, a gland involved by an extensive disease process like thyroiditis has a greatly reduced capacity to take up and fix iodine. It is interesting to note that the two adenomatous nodules studied did not take up iodine. It is always difficult to separate some involutionary nodules from true neoplastic adenomas, and perhaps the behavior of radioactive iodine may aid in the separation. If a larger series of cases were to demonstrate a consistent inability of true adenomas to take up iodine, then the question of their functional ability could probably be answered.

In 1942 Keston, Ball, Frantz and Palmer [9] described a femoral area of metastasis from a thyroid carcinoma which collected about 30 per cent of the administered iodine. At autopsy these authors [10] found that there were many areas of metastasis of undifferentiated thyroid tumor and that these did not take up radioactive iodine. The area of metastasis taking up substantial amounts was a well differentiated adenoma malignum. These authors also referred to a child patient in whom a colloid thyroid carcinoma had been removed and the presence of an area of metastasis taking up significant amounts of iodine established later. Leiter, Seidlin, Marinelli and Bauman [11] in 1946 described 2 patients in whom there was radioactive iodine uptake in metastatic thyroid lesions. One of these patients was thoroughly studied and reported on by Seidlin, Marinelli and Oshry.[7] This patient had extensive bony metastasis and pulmonary metastasis. By the use of large doses of radioactive iodine, the disease was apparently arrested.

9. Keston, A. S.; Ball, R. P.; Frantz, V. K., and Palmer, W. W.: Storage of Radioactive Iodine in a Metastasis from Thyroid Carcinoma, Science **95**:362-363 (April) 1942.

10. Frantz, V. K.; Ball, R. P.; Keston, A. S., and Palmer, W. W.: Thyroid Carcinoma with Metastases, Studied with Radioactive Iodine, Ann. Surg. **119**: 668-689 (May) 1944.

11. Leiter, L.; Seidlin, S. M.; Marinelli, L. D., and Bauman, E. J.: Adenocarcinoma of the Thyroid with Hyperthyroidism and Functional Metastases, J. Clin. Endocrinol. **6**:247-261 (March) 1946.

We believe that this observation of the failure of thyroid carcinoma to take up I^{181} deserves considerable stress. In only one of fifteen carcinomas was a significant iodine uptake demonstrable, and this carcinoma, in spite of its invasiveness, was relatively benign. The patient had had it for seventeen years. Sections of an invaded lymph node could hardly be distinguished from normal thyroid. The metastatic tissue was functioning in a normal manner so far as the production of thyroid hormone was concerned. In the series of fifteen carcinomas, only this benign carcinoma could possibly be considered for radioactive iodine therapy. However, even in this, certain areas had less uptake than others and therefore might not take up enough to receive adequate radiation. We believe that this series clearly indicates that radioactive iodine will be of limited value in the treatment of thyroid carcinoma.

Conceivably, some preliminary treatment might render the thyroid carcinoma or the areas of metastasis more amenable to iodine uptake. Theoretically, administration of thyrotropic hormone might possibly change the character of the carcinoma and make an appreciable uptake possible by rendering it hyperplastic. In this series, a metastatic nodule on the scalp of a patient who had undergone total thyroidectomy followed by extensive radiation to the thyroid area did not take up iodine. This patient showed mild hypothyroidism clinically. Presumably, increased amounts of circulating thyrotropic hormone were present because of the lack of much functioning thyroid tissue, and still the scalp nodule had no uptake. In some cases of surgically inaccessible thyroid metastasis, uptake in the area of metastasis could possibly be increased by performing a total thyroidectomy and waiting a short interval for the expected pituitary thyrotropic response before administering therapeutic radioactive iodine. The rationale for these procedures would be based on the observation of Keating and others [5] that the uptake of radioactive iodine could be increased by hyperplasia produced with thyrotropic hormone. Destruction of the thyroid could be done by means of radioactive iodine. After this initial treatment, the carcinoma tissue might then take up adequate radioactive iodine from a second dose and therapy could be considered. However, if the carcinoma had even small initial uptakes the thyroidectomy dose might damage it sufficiently to prevent further uptake while not checking the neoplastic growth.

SUMMARY

1. In the thyroid gland radioactive iodine is taken up in the glandular tissue, appearing both in the acinar epithelium and in the colloid.

2. In general the amount of uptake varies directly with the degree of hyperplasia in a gland undergoing the hyperplasia-involution cycle.

3. One simple adenoma and one fetal adenoma had small uptakes of radioactive iodine.

4. In cases of thyroiditis the iodine uptake is small and confined to the region least affected by the disease.

5. One of fifteen carcinomas demonstrated significant uptake of radioactive iodine. This carcinoma, along with pulmonary metastasis, had been present for twenty years and was extremely well differentiated and presumably putting out normal quantities of thyroid hormone.

6. Radioiodine will probably be of limited value as a sole therapeutic agent for treating carcinoma of the thyroid.

VOLVULUS OF THE COLON

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THE NOUN volvulus has its origin from the Latin verb "volvere" which means "to turn about" or "to roll." During the past one hundred years physicians have created and firmly established the word "volvulus" as a vernacularism common to their profession and without meaning if employed in any other manner. The term is interpreted as describing a process in which a torsion or twisting of a segment of bowel results in an obstruction to the lumen and a disturbance in circulation to the wall of the intestine.

Even though volvulus may occur almost anywhere in the gastrointestinal tract, this paper is designed primarily to deal with lesions of the colon. Eight cases of volvulus of the colon, encountered during the past ten years, form a basis for this study. A personal interest in volvulus of the colon was inspired by the rather unique experience of observing 5 of the 8 aforementioned cases during a brief period of three months.

While reviewing the literature, one is immediately impressed by the large series of cases and numerous articles on volvulus that appear in the foreign journals. In this country the number of cases in each report is relatively small, and in contrast to the European literature in particular, publications on volvulus of the colon appear much less frequently.

INCIDENCE

There exists a remarkable contrast between the incidence of volvulus of the colon in the United States and that in Europe, particularly in the Eastern and Nordic areas. In order that this contrast may be better understood, the following comparison is created. An analysis is made, based on the domestic publications [1] and the papers by European authors.[2]

From the Department of Surgery, George Washington University School of Medicine.

1. (*a*) Gilchrist, R. H.: Obstruction Due to Volvulus of the Colon, Arch. Surg. **56**:79 (Jan.) 1948. (*b*) Grace, A. J.: Volvulus of the Cecum, Canad. M. A. J. **38**:346 (April) 1938. (*c*) Griffin, W. D.; Bartron, G. R., and Meyer, K. A.: Volvulus of the Sigmoid Colon, Surg., Gynec. & Obst. **81**:287 (Sept.) 1945. (*d*) Hendricks, W., and Griffin, W. D.: Symposium on Clinical Advances in Surgery: Intestinal Obstruction; Analysis of Three Hundred and Fifty-Two Cases, S. Clin.

(Footnotes continued on next page)

For better understanding, a basic figure of 100 cases is used. This figure represents all types of obstruction of the large and small bowel regardless of origin and includes incarceration or strangulation of bowel associated with external hernias. It has been found in Europe that 40 cases, or 40 per cent, will result from volvulus and the remaining 60 cases, or 60 per cent, will be due to other causes. In the United States, however, only 7 cases, or 7 per cent will be due to volvulus, and 93 cases, or 93 per cent, will result from other factors. To carry the analysis further, in every 40 European cases of volvulus 10 cases, or 25 per cent, involve the small bowel and 30 cases, or 75 per cent, the colon, whereas in every 7 cases of volvulus in this country 4 cases, or 57 per cent, are known to involve the small bowel and 3 cases, or 43 per cent, the large bowel.

At this point, one may see that in every 100 cases of intestinal obstruction the incidence of volvulus of the colon is ten times as frequent in Europe as in this country.

For further consideration, still based on the original 100 cases, one finds that for every 30 cases of volvulus of the colon seen in Europe 10, or 33.3 per cent, will involve the cecum and 2, or 66.6 per cent, will involve the sigmoid. Higher percentages of involvement of the cecum have been reported. In Europe 17 per cent [2a] and in this country 5 to 6 per cent [1g] are about the top figures for cecal volvulus as a cause of intestinal obstruction, but they are well above the average. In 1938

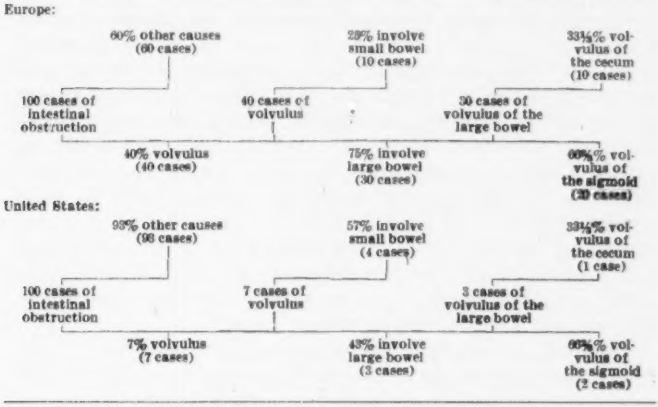
North America **27**:51-72 (Feb.) 1947. (*e*) Leonard, E. D., and Derow, S.: Volvulus: Study of Twenty-Two Cases, New England J. Med. **218**:388 (March 3) 1938. (*f*) Miller, J. M., and Clagett, O. T.: Volvulus of Ileocecal Region, Proc. Staff Meet., Mayo Clin. **15**:424 (July 3) 1940. (*g*) Pratt, J. P., and Fallis, L. S.: Volvulus of the Cecum and Ascending Colon: Report of Three Cases, J. A. M. A. **89**:1225 (Oct. 8) 1927. (*h*) Rothman, M.; Bruckner, J. P., and Zetena, D. F.: Volvulus of the Cecum and Ascending Colon, Am. J. Surg. **60**:292 (May) 1943. (*i*) Simon, H. E.; Senturia, H. R., and Keller, T. B.: Volvulus of the Sigmoid Colon, ibid. **71**:550 (April) 1946. (*j*) Sweet, R. H.: Volvulus of the Cecum, New England J. Med. **213**:287 (Aug. 15) 1935. (*k*) Wangensteen, O. H.: Intestinal Obstructions: A Physiological and Clinical Consideration with Emphasis on Therapy, Including Description of Operative Procedures, ed. 2. Springfield, Ill., Charles C Thomas, Publisher, 1942. (*l*) Weinstein, M.: Volvulus of the Cecum and Ascending Colon, Ann. Surg. **107**:248 (Feb.) 1938.

2. (*a*) Bona, T.: Volvulus of Cecum, Zentralbl. f. Chir. **65**:2425 (Oct. 29) 1938; The 1939 Year Book of General Surgery, Practical Medicine Series, Chicago, The Year Book Publisher, Inc., 1939. (b) Bruusgaard, C.: Volvulus of the Sigmoid Colon and Its Treatment, Surgery **22**:466 (Sept.) 1947. (*c*) Edgren, K., cited by Bruusgaard.[2b] (*d*) Laurel, H., cited by Bruusgaard.[2b] (*e*) Norgaard, F.: Periodic, Spontaneously Remittent Volvulus and the Symptoms in Cases of Colon Elongatum, Acta. radiol. **26**:163, 1945; Internat. Abstr. Surg. **83**:146, 1946; in Surg., Gynec. & Obst., Aug. 1946. (*f*) Peterson, L., cited by Bruusgaard. (*g*) Tuovinen, P., cited by Bruusgaard.[2b]

Grace [1b] reported that an extensive review of the literature failed to reveal any published case reports of volvulus of the cecum in Canada up to that time. In both Europe and the United States volvulus of the transverse colon is extremely rare. A possible explanation for the infrequency of involvement of this area will be brought out later. It may also be observed that in Europe volvulus is seen in the large bowel more frequently (75 per cent) than in the small bowel (25 per cent), whereas in this country the small bowel is found to be affected more often (57 per cent) than the large bowel (43 per cent).

Another interesting feature now becomes apparent. Even though volvulus of the large bowel occurs ten times as frequently in Europe as

TABLE 1.—*Cases of Volvulus in Europe and in the United States*


Europe:
60% other causes (60 cases)
25% involve small bowel (10 cases)
33⅓% volvulus of the cecum (10 cases)
100 cases of intestinal obstruction
40 cases of volvulus
30 cases of volvulus of the large bowel
40% volvulus (40 cases)
75% involve large bowel (30 cases)
66⅔% volvulus of the sigmoid (20 cases)
United States:
93% other causes (93 cases)
57% involve small bowel (4 cases)
33⅓% volvulus of the cecum (1 case)
100 cases of intestinal obstruction
7 cases of volvulus
3 cases of volvulus of the large bowel
7% volvulus (7 cases)
43% involve large bowel (3 cases)
66⅔% volvulus of the sigmoid (2 cases)

in this country, the ratio of volvulus of the sigmoid to volvulus of the cecum is 2:1 both here and in Europe.

To understand better the preceding statements, a comparative table is presented which shows the percentages and number of cases encountered in the study of every 100 cases of intestinal obstruction of all types. This analysis is based on the figures for Europe and the United States.

In over 90 per cent of the cases of obstruction of the large bowel in the United States the lesion is thought to be due to carcinoma.[1k] However, since there is no available evidence that carcinoma of the large bowel occurs with any less frequency in Europe than in this country and since over here it is recognized as one of the greatest causes of

obstruction of the colon, it seems safe to assume that the over-all frequency of obstruction of the large intestine must be much greater in Europe than in the United States. It is astonishing to review some of the figures for volvulus of the colon presented by foreign authors. In Norway, Sweden and Finland five authors [3] presented an enormous series of cases. When totaled, the following sum is obtained: 140 cases of volvulus of the cecum, 14 cases of volvulus of the transverse colon and 280 cases of volvulus of the sigmoid.

EMBRYOLOGY

In order to understand better the development of volvulus of the colon, a review of gastrointestinal embryology seems imperative. The primary alimentary canal appears about the fifth week of embryonic life and consists of three parts, the foregut, the midgut and the hindgut. The foregut ultimately becomes the stomach and duodenum, whose blood supply is derived from the celiac axis and whose physiologic function is chiefly one of digestion. The midgut forms the small intestine, right side of the colon and right half of the transverse colon. The function becomes one of absorption, and the blood supply is from the superior mesenteric vessels. The midgut may be divided into two parts, that portion proximal to the site of the vitelline duct (the origin of Meckel's diverticulum and other omphalomesenteric disorders), which is called prearterial, and the remaining distal half, referred to as postarterial. The hindgut makes up the remainder of the alimentary canal. It consists of the left transverse colon and the entire left side of the colon. The blood supply is via the inferior mesenteric vessels, and, physiologically speaking, it is an organ of excretion.

The cecum appears as a budlike process in the postarterial portion of the midgut at about the sixth week of embryonic life. At this time much of the intestine is in the base of the umbilical cord. At approximately the tenth week the intestine is withdrawn into the abdomen, with the cecum coming to rest in the upper portion, just beneath the stomach. By rotation, the cecum gradually moves to the right upper quadrant and then on to the right lower quadrant. At this time the mesenteries of the cecum and the ascending colon and the left side of the colon down to the sigmoid area become fused to the posterior abdominal wall.

It becomes evident that arrests in development during fetal life may result in (*a*) an incompletely rotated cecum, (*b*) failure of attachment of the mesentery along the posterior abdominal wall and (*c*) a completely rotated, but mobile and unattached cecum. The last two factors are particularly significant in a consideration of volvulus of the large bowel.

3. Bruusgaard.[2b] Edgren.[2e] Laurel.[2d] Peterson.[2f] Touvinen.[2g]

ETIOLOGY

From the standpoint of etiology, the predisposing factors and the acquired or exciting factors must be considered. Certain predisposing factors must be present in order that a volvulus may occur. Among these factors are (*a*) elongation of the mesentery with a freely movable bowel; (*b*) absence of the mesentery with a mobile bowel; (*c*) closely approximated points of fixation, and (*d*) limbs of the bowel close together.

Normally there is fixation of the right side of the colon and the cecum. However, it has been reported [1h] that from 13 to 32 per cent, or an average of 20 per cent,[11] of all persons have an ascending mesocolon or an unattached cecum. It was noted in a consideration of embryology that arrested fetal development may give rise to this. It is believed that such anomalies occur more frequently in women.[1h] An explanation of the relative infrequence of cecal volvulus is due to the normal tendency for fixation of this part.

Volvulus of the transverse colon is almost a rarity. It has been pointed out[1k] that the points of fixation, namely, the splenic and hepatic flexures, are so far apart as to make a twisting, even in the presence of enteroptosis, practically impossible.

The sigmoid area is the site most frequently involved in cases of volvulus of the large bowel. Here again, one may revert to embryology for clarification. Shortly after the eleventh week of fetal life the mesentery of the left side of the colon, from the splenic to the sigmoid flexure, fuses to the posterior abdominal wall. Since this fusion may extend a little into the sigmoid area, the predisposing factors of an elongated mesentery, freely movable bowel, narrow point of fixation and limbs of bowel in close approximation are thus created.

It would appear that the acquired or exciting etiologic factors are not too well understood. Diets high in vegetables and residue and the diets in countries on war rations, both of which have been in use in the eastern European area, appear to be the most popular factor for the precipitation of volvulus formation.[2b] External and internal injury from trauma, severe purgation, overexertion and heavy eating have been mentioned as possibly associated with volvulus.[11] There are some who feel that pregnancy plays a part in the formation of volvulus,[1b] while others say that it acts to prevent the onset.[2b] Megacolon may well play a part, but some writers [4] are of the opinion that a vicious cycle exists in that attacks of volvulus of the sigmoid may occur and give rise to a megacolon, which in turn tends to result in a volvulus less likely to undergo spontaneous reduction. Tumors, fecaliths and foreign bodies have also been suggested [1h] to play a part. It has been impossible

4. Scott, W. J. M., and Serenati, Q. J.: Megacolon: Mechanism and Choice of Treatment, Surgery **20**:603 (Nov.) 1946.

to find any mention of paralytic ileus as an exciting factor. However, as will be seen in case 2 reported herein, paralytic ileus definitely seems to be an exciting factor in the formation of volvulus.

PATHOLOGIC PROCESS

As has been previously mentioned, volvulus is by definition a mechanical derangement of the intestine which may result in obstruction of the lumen, circulatory changes in the wall or a combination of the two. One may readily understand that torsion of the bowel alone may cause some narrowing of the lumen by impingement. However, an additional factor has been pointed out which better accounts for the completeness of the obstruction. There is definite evidence [5] that every torsion of a segment of bowel and its mesenteric axis is associated with an axial torsion of the bowel itself about a point of posterior fixation. This axial torsion is twice as great as the torsion of the mesentery. Therefore, in a case of volvulus of 180 degrees there is created an axial twist of 360 degrees which may completely occlude the lumen.

The circulatory change in the wall of the intestine in a closed loop obstruction associated with volvulus is one of early venous occlusion which results in damage to the wall of the bowel and marked losses in blood volume.[1k] It has been suggested recently [6] that reflex arterial spasm may account for the vast difference in the prognosis of the viability of a strangulated bowel resulting from arterial occlusion as contrasted with one due to venous occlusion. The latter, a type seen in volvulus, tends to show irreversible damage of the wall much earlier than the other, which is probably seen clinically only in cases of true arterial embolism or thrombosis.

Next, one must consider the development of gaseous distention resulting from closed loop obstruction and circulatory damage. Swallowed air is not an important factor as a source of gas in distention of the large intestine. The gaseous content in clinical cases of obstruction of the large bowel has been shown to be made up of the following percentages: nitrogen, 72 per cent; oxygen, 2 per cent; carbon dioxide, 10 per cent; hydrogen, 6 per cent; methane, 1 per cent, and hydrogen sulfide, 9 per cent.[1k]

In cases of volvulus, in which obstruction is combined with a compromised blood supply and an arrest of venous outflow from the bowel, the two main sources for gas formation are (*a*) diffusion of blood gases, especially nitrogen, into the lumen and (*b*) gaseous products of decomposition and putrefaction within the bowel.

Unrelieved intraluminal tension has a deleterious mechanical effect on the wall of the bowel, but the entire colon tolerates distention better

5. Groth, K. E., cited by Bruusgaard.[2b]

6. Laufman, H., and Method, H.: The Role of Vascular Spasm in Recovery of Strangulated Intestine, Surg., Gynec. & Obst. **85**:675 (Dec.) 1947.

than does the small intestine. As soon as venous obstruction takes place sufficiently to alter the viability of the wall of the bowel, marked loss of blood into both the lumen and the wall results, and the wall becomes permeable to pathogenic organisms and toxins. Surgical shock and peritonitis soon follow.

CLASSIFICATION

Terms have been employed in describing a volvulus of the colon, among which are such words as "periodic," "recurrent," "intermittent," "spontaneously remittent," "chronic," "subacute," "incomplete" and "complete." It has been mentioned [7] that a volvulus of less than 180 degrees may be considered "physiologic," but when the torsion is greater than 180 degrees it becomes "pathologic." It is apparent that the degree of mechanical involvement constitutes the basis for this suggestion.

It has been brought out earlier in this paper that certain predisposing factors must exist in order that a volvulus may occur, and when it does occur the pathologic changes are the direct result of a torsion of the bowel. Here there is a basis for a classification of volvulus of the colon that could be standardized under the heading of (*a*) anatomic location and (*b*) extent of pathologic changes. The pathologic changes may be graded from 1 to 4, depending on the extent of involvement.

Grade 1 designates a volvulus of less than 180 degrees which is asymptomatic and is discovered incidentally by roentgenologic studies after a barium enema. The importance of this is that the conditions are present that predispose to further torsion and therefore a higher gradation of volvulus may develop.

Grade 2 designates a volvulus of more than 180 degrees with a partial obstruction which either tends to untwist spontaneously, or can be decompressed by means of proctoscopy, rectal tube, change of position or enemas. In other words, a grade 2 volvulus can temporarily be relieved by conservative measures.

Grade 3 is the classification given to a volvulus of more than 180 degrees resulting in an irreversible, complete obstruction with formation of a "closed loop." However, circulatory damage, if present, is reversible, and the bowel is viable.

Grade 4 designates a volvulus of more than 180 degrees with an irreversible complete closed loop intestinal obstruction and irreparable circulatory damage to the bowel.

By this method of classification a process is more readily explained. In other words, a patient may go through any of the gradations of volvulus. For example, he may have grade 1 volvulus unknowingly. Then the disease may fall into the category of grade 2, but the patient spontaneously recovers from attacks. Next grade 3 volvulus may develop, but at operation, which becomes mandatory, the bowel is found

7. Wilms, M., cited by Bruusgaard,[2b] Norgaard.[2e]

to be viable. If operation is delayed, grade 4 volvulus may occur, in which the bowel has become gangrenous.

In summary, the word volvulus designates the type of lesion, terms like cecum, sigmoid and ascending colon determine the anatomic location and the grades, 1 to 4, reveal the extent of the pathologic changes.

After the case reports, which appear next, an attempt will be made to tabulate and summarize the findings, and each case will be graded as suggested in the classification just discussed.

REPORT OF CASES

CASE 1.—S. R., a 43 year old white woman, was hospitalized on May 7, 1943. The past history revealed that the patient had not undergone a previous abdominal

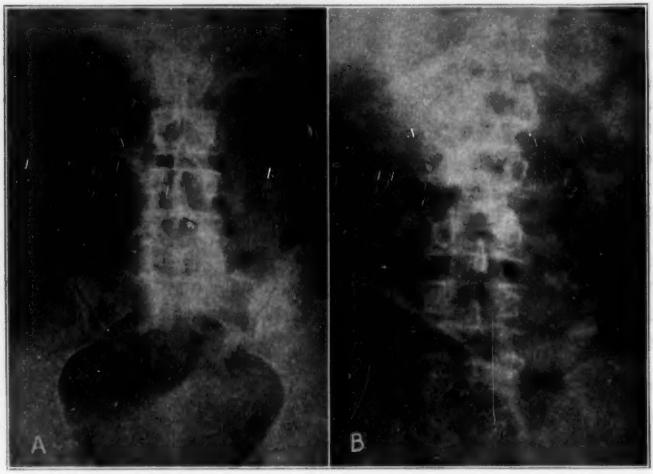


Fig. 1.—*A*, roentgenogram of the patient presented in case 1. Note the enormous dilatation of the right side of the colon and of the loops of the small bowel. Volvulus of the cecum. *B*, roentgenogram of the patient in case 2. Note the enormous dilatation of the right side of the colon which fills the right area of the abdomen and pelvis. Distention of the small bowel is rather marked. Volvulus of the cecum.

operation. The menstrual history was normal. She had had three children. The present illness was characterized by the suddenness of its onset. Twenty-four hours prior to her admission, the patient was perfectly healthy. About twelve hours before admission she began to have severe pain in the right abdominal area, nausea, vomiting and constipation and was unable to expel gas.

Examination revealed a distended abdomen which was tender on the right side. The general appearance was one of mild shock. The pulse rate was 140, the blood pressure 90 systolic and 60 diastolic and the temperature 98 F. The pelvic examination revealed no abnormalities. A roentgenogram, shown in figure 1*A*, revealed a large distended bowel on the right side.

Operation was performed about three hours after admission. The abdomen was opened through a long right paramedian incision. The right side of the colon and about 12 inches (30 cm.) of the distal portion of the ileum were involved in complete torsion of a clockwise nature, over 360 degrees. There was a long mesentery to the right side of the colon, which became short at the site of the hepatic flexure. After detorsion the ileum was sutured to the transverse colon. Even though viable, the right side of the colon and the terminal portion of the ileum were resected between clamps. The abdomen was then carefully closed about the clamped ends of the ileum and colon. A large rubber tube was sutured into the ileum after the clamp was first removed. After a relatively uneventful course, a spur clamp was inserted into the lumen of the ileum and colon on May 18, 1943, the eleventh postoperative day. The clamp cut through in about five days, after which the patient was discharged from the hospital. She returned in August of 1943, at which time an extraperitoneal closure of the ileum and colon was carried out.

The patient was found to be in good health in September of 1947, over four years after her last operation.

Case 2.—D. O., a 45 year old white man, was hospitalized on Jan. 4, 1947, with a history of an injury in which he sustained a fracture of the left hip. During the first forty-eight hours after his admission he was fairly comfortable, but at the end of this period he began to have abdominal distention and the percussion note was tympanitic. As yet there was no pain, nausea or vomiting. Because of the complication, the anticipated hip-nailing operation on the left femur was postponed. The distention remained the same for about three days, and after supportive measures and frequent enemas the patient was able to expel some gas. On the evening of the fifth day after his admission he was no longer able to expel any gas with enemas. He began to have abdominal pain, which increased during the night and the following day, and he became nauseated and vomited. There was no evidence of previous gastrointestinal disturbances in this patient.

Physical examination revealed a markedly distended abdomen, with diminished bowel sounds, tympanitic percussion note and increasing tenderness in the right lower quadrant. The hemoglobin content was 87 per cent, the red blood cell count 4,300,000, the white blood cell count 10,000, the pulse rate about 100 and the temperature normal. The roentgenogram shown in figure 1*B* represents a tremendous dilatation of the right side of the colon.

At operation on Jan. 10, 1947, a 180 degree volvulus of the cecum, terminal portion of the ileum and ascending colon was encountered. The wall of the intestine was dusky and edematous. However, after detorsion and decompression the color seemed to return to normal. Exteriorization was carried out on the involved bowel, which was later cut away. The patient did well postoperatively during the first eleven days. However, after this time he began to bleed rather profusely from the spur that had been crushed with a clamp. This hemorrhage was easily controlled, and the lowered blood volume was returned to normal by the use of transfusions. After this he had no further complications. On Feb. 19, 1947, the fracture of the neck of the left femur was nailed.

The postoperative course was satisfactory, and the patient was discharged on March 4. He was readmitted to the hospital on June 16, at which time an extraperitoneal closure of the fistula was performed. He has remained well and was symptom free on October 15, 1948.

Case 3.—E. W., a 51 year old white woman, was hospitalized on March 5, 1947. Her past history revealed that she had had tuberculosis in 1924, which

had been controlled. She had suffered considerably from seasonal asthma for many years. In September 1946, just six months prior to her admission, she had undergone an appendectomy. Significant is the fact that the appendectomy did not relieve the abdominal discomfort from which she had been suffering for several years, as the identical pains were still present after operation. The present illness began about fourteen hours prior to her admission, consisting of pain which was more or less generalized, intermittent in character and recurring every ten or fifteen minutes. Six hours after the onset of pain she began to have nausea and vomiting. The patient had had no stool during the past forty-eight hours and had not expelled any gas for the past twenty-four hours. Examination revealed a sick-looking patient. Roentgenograms were taken, which are shown in figure *2A*. The abdomen was moderately distended. Bowel sounds were audible. The

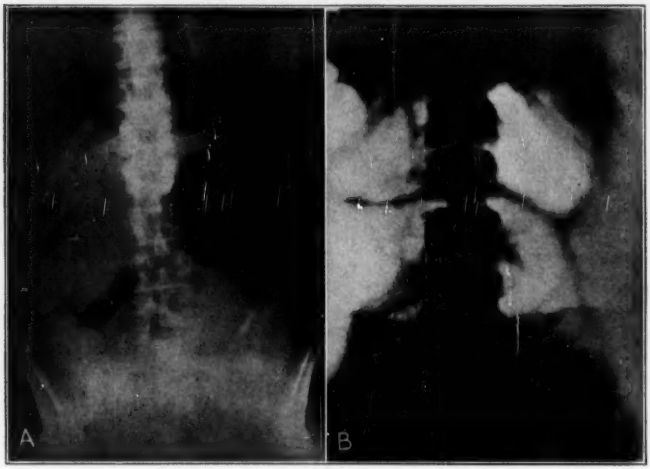


Fig. 2.—*A*, roentgenogram of the patient in case 3. Note the dilatation of the cecum and its location in the upper left quadrant of the abdomen with its fluid level. The gastric shadow can be seen just above the cecum and the distended terminal portion of the ileum coming up from the right lower quadrant. Volvulus of the cecum. *B*, roentgenogram of the patient in case 4. Note the enormously dilated bowel which has pushed transversely from left to right. Few small bowel shadows are seen. Volvulus of the sigmoid.

pulse rate was 100, the blood pressure 120 systolic and 80 diastolic, the white blood cell count 13,000, the red blood cell count 4,500,000 and the hemoglobin content 80 per cent.

Within six hours after her admission the patient was taken to the operating room. At operation a large, clockwise, 360 degree volvulus of the cecum and terminal portion of the ileum was found. The greatest portion of this volvulus was located in the upper left region of the abdomen. The wall of the bowel appeared to be viable. The entire redundant portion was exteriorized and clamps applied. A decompressing tube was put into the terminal portion of the ileum

and the bowel cut away. The clamps on the bowel were allowed to slough away. After about ten days a spur clamp was inserted over the septum that had been created between the ileum and the transverse colon. On April 8, 1947, the patient was taken to the operating room and closure of the external ileocolic fistula was carried out. She was completely relieved of the abdominal symptoms which had persisted for many years. An accurate follow-up has been carried out, because carcinoma of the breast has since developed and she has been under close observation after a radical mastectomy. The last follow-up examination was on Sept. 17, 1948.

CASE 4.—C. M., a 48 year old Negro, entered the hospital on Aug. 2, 1939, because of severe abdominal pain. He stated that his past health had been good. He was accustomed to having a bowel movement every day and had not been troubled with attacks of abdominal pain. His present illness began on July 30 1939, when he did not have a bowel movement. At noon of the following day, thirty-six hours prior to his admission, he began to have some abdominal pain which he described as "cramplike." However, it was not until twelve hours before he entered the hospital that he began to vomit, and the pain increased markedly. He took several enemas without benefit.

Physical examination revealed a moderately ill, middle-aged man with a tremendously distended abdomen. The percussion note was tympanitic throughout. There was no definite palpable masses. Occasional tinkles could be heard in the bowel. The blood pressure was 100 systolic and 60 diastolic, the temperature 99 F. and the white blood cell count 7,900. Examination of the urine showed it to be normal. The nonprotein nitrogen was 34 mg. The pulse rate was 120. An enema was returned without coloring or flatus. A roentgenogram of the abdomen was taken and is shown in figure *2B*. A preoperative diagnosis of a complete obstruction of the large bowel was made.

The abdomen was opened through a left paramedian incision, and a loop of twisted sigmoid colon suddenly extruded. The caliber of the intestine was larger than the calf of a man's leg and gave the appearance of an inflated inner tube of a tire. The enlarged distended bowel, even though dusky in color, appeared to be viable. An examination of the vessels to this part disclosed no evidence of thrombosis. There was a 270 degree counterclockwise torsion of the bowel. When this was rectified, the proximal portion of the colon, which was not appreciably distended, suddenly filled with gas and somewhat deflated the involved segment bowel. A rectal tube was inserted, and a tremendous amount of flatus was expelled. Since the patient's general condition was poor, it was decided to suture the mesentery to the lateral wall and perform a cecostomy through a McBurney type incision on the right side. After this the abdomen was carefully closed in layers.

The postoperative period was rather uneventful. The temperature, pulse and respiration returned to normal, and the cecostomy opening began to perform well. The patient left the hospital on the fourteenth postoperative day. On Dec. 26, 1939, over four months after the operation, he again presented himself with abdominal pain and symptoms of mild incomplete obstruction. It was learned that he had been indiscreet about his diet. String beans and other substances were recovered from the cecostomy opening. By irrigation, and with the aid of indwelling Miller-Abbott tube, decompression was carried out and obstruction relieved. It was at this time that the patient was advised to undergo resection

of the sigmoid colon. He absolutely refused any further surgical treatment, even closure of the cecostomy opening. It has been learned that he died about a year and a half later, in June 1941, from a recurrence of the volvulus.

Case 5.—E. C., a 69 year old Negro, was hospitalized on Dec. 24, 1946. A complete past history was not elicited because of the poor general condition of the patient. Apparently the present illness was of forty-eight hours' duration, characterized by severe abdominal pain, vomiting and distention. He had had loose stools on two occasions, accompanied with gas which did not bring relief, after which obstipation ensued. The patient stated that the pain had begun first in the back and had worked around to the abdomen in the region of the umbilicus. Physical examination revealed the abdomen to be markedly distended. There was generalized direct and rebound tenderness, and a tense sausage mass was

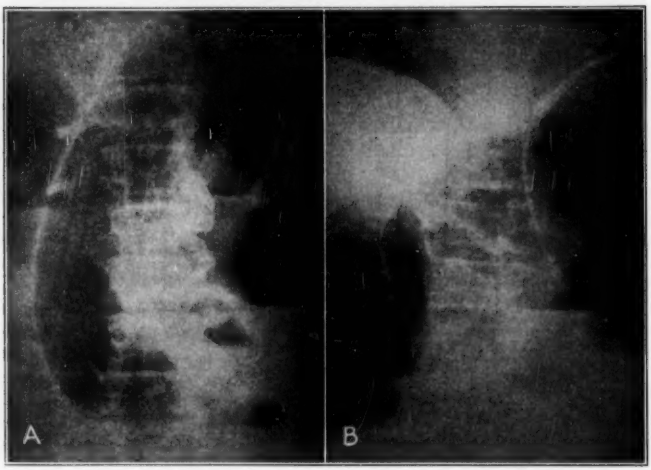


Fig. 3.—*A*, roentgenograms of the patient in case 5. Note the enormously dilated elongated segment of bowel which fills the greater part of the abdomen. Volvulus of the sigmoid. *B*, roentgenogram of the patient in case 6. Note the numerous markedly dilated segments of large bowel containing fluid levels. It is interesting that this bowel was found to be viable and an interval of ninety-six hours transpired between the onset of pain and the time of operation. This patient gave a history of recurring abdominal pain and constipation for the past twenty years. Volvulus of the sigmoid.

present in the left side of the abdomen. Peristalsis was absent, and metallic tinkles could be heard. Arteriosclerosis of the peripheral arteries was marked. The temperature was 98 F., the pulse rate 144, the respiratory rate 36 and the blood pressure 80 systolic and 60 diastolic. A roentgenogram of the abdomen is shown in figure 3*A*. Immediate supportive measures were instigated, but the patient failed to respond, and he died before operative intervention could be carried out.

Postmortem Findings.—A large counterclockwise volvulus of about 360 degrees involving the sigmoid was found. The bowel was completely gangrenous. The gangrene extended low down into the rectum, as the superior hemorrhoidal vessels were completely thrombosed.

Case 6.—L. S., a 48 year old Negro, was hospitalized on Dec. 27, 1946. He gave an interesting past history, complaining that he had had attacks of abdominal pain sometimes lasting from two to three days for over twenty years. The pains were intermittent in character and would soon subside. During the interim, he would feel well. His past history was otherwise noncontributory. Four days prior to his admission he started to have abdominal pains similar to those he had been accustomed to having in the past. The pains were at intervals of about every forty-five minutes but seemed to grow progressively worse. After having them for about twenty-four hours, he stopped expelling flatus and became constipated. The abdomen was markedly distended, and about twenty-four hours prior to his admission to the hospital he began to vomit, something that he had never done with the previous attacks of pain.

Physical examination showed the abdomen to be distended to enormous proportions. The bowel sounds were not audible, but there were succussion splashes. The pulse rate was 110, the blood pressure 130 systolic and 80 diastolic and the temperature 99 F. The roentgenogram is shown in figure 3*B*. Shortly after his admission the patient was taken to the operating room, and a decompressing transverse colostomy was performed. He stood the procedure well and improved rapidly. On Feb. 19, 1947, he was again taken to the operating room, and the entire redundant sigmoid was resected. Again the postoperative course was relatively uneventful, and at the last follow-up examination, about a year and a half after his discharge from the hospital, he was found to be well and symptom free.

Case 7.—H. P., a 64 year old Negro, was hospitalized on Jan. 24, 1947. His past history was one of relatively good health. He had had an accident some years ago, at which time he sustained several fractures. There was a history of an attack of pneumonia about one year previously from which he promptly recovered. The present illness was marked by a rather fulminating onset. Until Jan. 23, 1947, the patient felt well. During the night he had several watery stools which were soon followed by generalized pain in the abdomen. This continued throughout the night, and on the next morning the patient began to vomit. The pain and vomiting became worse. When seen on the evening of January 24, shortly after his admission, the patient was in shock. The abdomen was tympanitic, distended and resistant. He complained of a feeling of fulness. No bowel sounds could be heard. The blood pressure was 60 systolic and 40 diastolic and the pulse rate about 140. A roentgenogram of the abdomen is shown in figure 4.

The next few hours were energetically used in preparing the patient for operation. When the pulse rate and the systolic blood pressure improved, he was taken to the operating room. The abdomen was opened through a left paramedian incision and an enormous loop of the left side of the colon, the sigmoid and the upper region of the rectum were found to be involved in a volvulus of 360 degrees. There was thrombosis of all the left colic vessels extending down to and including the superior hemorrhoidal vessels. Because of the wide distance between the proximal and distal ends of the viable bowel, exteriorization could not be carried out. The proximal portion, which was clamped, was brought out through the

superior part of the incision. The inferior portion was clamped and was dropped back after the peritoneum was hurriedly split and resutured anteriorly.

Postoperatively, the laboratory reports and clinical observations indicated that the patient seemed to be holding his own during the first six days. However, on the sixth day, the pulse rate again rose to 140 and the respiratory rate became 40 per minute. The temperature, which had remained normal for six days, rose to 101 F. and then gradually over the next five days to 105 F. The patient died at 7:00 a. m. on Feb. 4, 1947, the eleventh day after the operation. Autopsy revealed that the abdominal findings were more or less negligible and that the cause of his death was extensive bilateral bronchopneumonia.

Fig. 4.—Roentgenogram of the patient in case 7. Note the enormously dilated large bowel. There is one area of dilatation of the small bowel present. Volvulus of the sigmoid.

CASE 8.—C. M., a 54 year old Negro, was hospitalized on Nov. 21, 1940, because of abdominal pain and fulness. The past history revealed that he had had occasional constipation. He had never taken an enema but frequently took laxatives. The onset of the present illness was thirty-six hours prior to his admission, when he first noticed abdominal pain and constipation and soon thereafter was unable to expel gas. There was a feeling of tremendous fulness in the abdomen. It was not until about eight hours prior to his admission that he began to vomit. An enema given immediately on admission was ineffectual. Examination revealed a thin, middle-aged white man in moderate distress and looking ill. On inspec-

tion of the abdomen, the left side seemed to be much fuller than did the right. The percussion note throughout was tympanitic. Little material was obtained from the stomach when a large caliber tube was inserted. The pulse was rapid and weak; the blood pressure was 90 systolic and 60 diastolic. Because of difficulties with technical equipment preoperative roentgen examination was impossible.

An impression of acute obstruction of the bowel was entertained, and the patient was taken to the operating room, where, under general anesthesia, a left paramedian incision was made to open the abdomen. Immediately encountered was a large loop of sigmoid which was gangrenous. It was so distended that the serosal layer had split in many places. The bowel was exteriorized from the abdominal cavity. Numerous areas of thrombotic vessels could be seen. The bowel was almost black in color. Clamps were applied to viable bowel proximal and distal to the torted loop, and the gangrenous segment cut away. The gangrene had involved such a large segment that it was impossible to approximate the two ends of viable bowel in the wound. Therefore it was necessary to bring the proximal portion out of the superior end of the incision and the distal portion out of the inferior angle.

The immediate postoperative course was rather stormy, the temperature ranging from 101 to 103 F. and the pulse rate from 120 to 130, with the respiratory rate about 30. However, on the fifth postoperative day the patient began to improve. The proximal loop began to function well, and he was discharged on Dec. 23, 1940. A follow-up examination in February 1947 revealed that the patient had a well-functioning colostomy opening and was in excellent health.

COMMENT ON CASES REPORTED

From the detailed case reports and table 2 the following findings are reviewed. In cases 1, 2 and 3 the cecum was involved. All the patients were white, and 2 of them were women. The average age was 46 years. The average time interval between onset of pain and operation was seventeen hours. These persons did not look extremely ill. The bowel was viable in all 3 instances, and a resection of the involved area was performed. The patients are well and symptom free at the time of this writing.

In cases 4, 5, 6, 7 and 8 the sigmoid was involved. It is of interest that the patients were Negroes whose average age was 56 years. The interval between the onset of pain and the time of operation was an average of fifty hours. Three of the 5 patients presented gangrene of the involved bowel. There were three resections and one decompression, detorsion and simple fixation. One patient was so moribund on admission to the hospital that operation could not be performed. Of these 5 patients, 2 are well today. One patient was well for a year and a half after discharge from the hospital but died of a volvulus at a later date. It is not difficult to understand how this occurred because the patient, when advised to have a resection, refused to undergo any further surgical procedure, even closure of the cecostomy opening. There were 2 deaths in the hospital. One patient died shortly after admission, having been brought to the hospital in a moribund state.

TABLE 2.—*A Brief Summary of the Findings in the Eight Cases Reported*

Factors:	Case 1 (SR)	Case 2 (DO)	Case 3 (EW)	Case 4 (CM)	Case 5 (EC)	Case 6 (LS)	Case 7 (HP)	Case 8 (CM)
Age	43	45	51	48	69	48	64	54
Race	W	W	W	N	N	N	N	N
Sex	F	M	F	M	M	M	M	M
Admission date	May 7, 1943	Jan. 4, 1947	March 5, 1947	Aug. 2, 1939	Dec. 24, 1946	Dec. 27, 1946	Jan. 24, 1947	Nov. 21, 1940
General condition	Mild shock	Good but became ill	Appeared ill	Moderately ill	Moribund	Moderately ill	Severe shock	Severe shock
Previous abdominal operations	None	None	Appendectomy 6 mo. before	None	None	None	None	None
Previous abdominal symptoms	None Grade 1	None Grade 1	Yes,* for many years Grade 2	None Grade 1	None†	Pains and constipation 20 yr. Grade 2	None Grade 1	No pain but did take laxatives for constipation Grade 2
Duration of pain, hours	12	24‡	14	36	48	96	24	36
Grade of volvulus	3	3	3	3	4	3	4	4
Site of lesion	Cecum	Cecum	Cecum	Sigmoid	Sigmoid	Sigmoid	Sigmoid	Sigmoid
Condition of bowel and degree of torsion	Viable 180°	Viable 180°	Viable 360°	Viable 270°	Gangrenous 360°	Viable	Gangrenous 360°	Gangrenous
Type of treatment	Obstructive resection	Obstructive resection	Obstructive resection	Decompression, detorsion and fixation		Immediate decompression, later resection	Obstructive resection	Obstructive resection
Follow-up	Well 4 yr. later (September 1947)	Well 1½ yr. later (October 1948)	Well 1½ yr. later (September 1948)	Well 1½ yr. and died after recurrence§	Died immediately after admission	Well 1½ yr. later (August 1948)	Died 11th postoperative day; bronchopneumonia	Well 6 yr. later (February 1947)

* Since this patient was already in the hospital, the twenty-four hour period indicates the interval between the onset of abdominal pain and the time of operation.

† The recent appendectomy had been performed because of symptoms identical with those present on admission.

‡ It is important to recall that this patient had been encouraged to undergo sigmoid resection. He supposedly died of a recurrence, in that the cecostomy was never closed.

§ This patient was so moribund on admission that a past history was not obtained.

The other patient died on the eleventh postoperative day after an initial postoperative course which was satisfactory and indicated improvement. At the postmortem examination extensive bilateral bronchopneumonia was present.

In only 2 of the 8 cases did the past history indicate that there had been previous similar complaints. The patient in case 3 had undergone appendectomy because of complaints which had persisted for many years. The patient in case 6 complained of abdominal pain and constipation over a period of twenty years. No information could be obtained in regard to the past history in case 5. In case 8 there was no history of pain, and the patient never had to take enemas. However, he did confess that he frequently took laxatives for mild constipation.

In case 6 the time interval between the onset of abdominal pain and the time of operation was ninety-six hours. The roentgenogram shown in figure 3 *B* reveals a tremendous amount of distention of the bowel and many fluid levels. At operation the intestine was still viable. It may seem feasible to speculate that a grade 2 volvulus had existed over a twenty year period and had created a megacolon, as had been mentioned,[4] thus making it possible for the patient to tolerate the obstruction better than the other patients who came to the hospial after a much shorter period after the onset of pain.

The short interval between the time of onset of abdominal pain and the time of operation in the patients who had a volvulus of the cecum can best be understood on the basis of the obstruction created in the terminal portion of the ileum which hastened the onset of nausea, vomiting and other symptoms. In the cases of sigmoid lesions vomiting was late, as is expected in instances of obstruction of the large bowel, and the time interval between the onset of pain and operation was considerably longer. However, 3 of the 5 patients presented themselves with gangrene of the bowel, and the entire group of 5 patients in whom the sigmoid was involved appeared considerably more ill than did those in whom the cecum was involved.

Under the proposed gradation system all 8 cases might have been grade 1, since it was possible for volvulus to develop on account of the presence of certain predisposing factors. Had barium studies been made of these patients at any time, the predisposition may have been discovered. There was no history indicative of grade 2 involvement in cases 1, 2, 4, 5 and 7; however, one is led to believe that volvulus may have accounted for the previous symptoms in cases 3, 6 and 8. Operation in cases 1, 2, 3, 4 and 6 showed what was considered to be grade 3 volvulus. All these patients survived operation. In cases 5, 7 and 8 the volvulus was considered to be grade 4, and only 1 patient survived. From these cases one would surmise that grade 3 volvulus of either

the sigmoid or the cecum carries a relatively good prognosis but that when grade 4 volvulus develops with the associated gangrene, the outlook becomes grave.

It would appear that the mortality rate for volvulus of the colon depends more on the degree of the process than on the site of involvement.

SIGNS AND SYMPTOMS

In general, when articles are written about volvulus of the colon, the authors mention that the cecum and sigmoid areas may be involved. However, the tendency is then to elaborate on one of the two conditions at the expense of the other. It has been attempted throughout this paper to consider volvulus of both the cecum and the sigmoid as equally as possible and contrast or compare them in every feasible manner. The site of an obstructive lesion of the bowel has an important influence on the effects of that obstruction. We have mentioned grade 1 volvulus of the cecum or sigmoid, but aside from its potentialities it is of no immediate concern since it is nonsymptomatic and is discovered accidentally.

The grade 2 volvulus of the cecum and sigmoid is important. The symptoms may merely be attacks of pain and some distention which is relieved by enemas or change of position. This stage apparently occurs more frequently than is realized [8] and may constitute a good warning of what might follow. It has been stressed that this type of volvulus of the cecum has frequently precipitated an incorrect diagnosis of "chronic appendicitis," for which an appendectomy has been performed, without improvement.[9] Case 3 presented in this report is a good example.

The signs and symptoms of grade 3 volvulus of the cecum are predominantly those associated with low obstruction of the small bowel. The onset of symptoms is usually rapid. The early pain is manifested by frequent cramplike contractions, which become more continuous as distention takes place and traction on the mesentery occurs. The distention as a rule is only of a moderate degree, because the segment of bowel involved is relatively small. Nausea and vomiting may result and soon become severe. Constipation follows, but some fecal material and flatus in the distal colon may be expelled before complete obstipation ensues. Dehydration takes place relatively early and may become

8. Holmgren, B. S.: Volvulus, Acta. radiol. **19**:230 (Sept.) 1938; The 1939 Year Book of General Surgery, Practical Medicine Series, Chicago, Year Book Publishers, Inc., 1939. Grace.[1b] Griffin and others.[1c] Hendricks and Griffin.[1d] Sweet.[1j]

9. James, K. L.: Volvulus of Pelvic Colon in Young Person, Brit. M. J. **2**:569 (Sept.) 1938. Bona.[2a] Grace.[1b] Sweet.[1j]

marked unless combative measures are instigated. A scout roentgenogram of the abdomen may reveal only the distended closed loop of torted bowel and some dilatation of the small bowel. Incidentally, the involved cecum may be located anywhere in the abdomen. In figure 2*A* the cecum is seen in the left upper quadrant. This same picture shows only a relatively scanty amount of distention of the small bowel. However, an earlier roentgenogram, taken prior to the introduction of a tube into the stomach, showed considerably more gas in the small bowel. It is felt that some of the distention in volvulus of the cecum may be reduced by use of the Miller-Abbott tube. A barium enema study will usually reveal little more than just the site of the obstruction and may be a rather dangerous procedure from the standpoint of possible perforation.

TABLE 3.—*Signs and Symptoms of Grade 3 Volvulus*

Site	Cecum	Sigmoid
Type	Small bowel	Large bowel
Onset	Sudden	Gradual
Pain	Almost continuous	Intermittent and cramplike
Distention	Moderate	Marked
Vomiting	Early and severe	Late
Constipation	Considerable	Considerable, but may be preceded by diarrhea
Dehydration	Early	Later
Flat plate roentgenogram	Small bowel is distended as well as closed loop; of some aid after use of Miller-Abbott tube	Small bowel is not distended due to ileocecal competency; the colon proximal is distended; of no aid after use of Miller-Abbott tube
Barium study	Of little aid except to show where obstruction is located	May show: (1) location of obstruction; (2) length of segment involved; (3) degree of obstruction of lumen, or (4) just "ace of spades" appearance

The clinical manifestations seen in patients with grade 3 volvulus of the sigmoid are chiefly those associated with obstruction of the large bowel. The onset of symptoms is more or less gradual. Pain at first may be intermittent, and there may be a considerable period between the paroxysms. Occasionally patients may have a severe backache as their only pain.[11] One would assume that this could result from the traction on the mesentery. In case 5 of this series the symptoms began with a backache. Distention may become severe, with tremendous dilatation of the loop. Nausea and vomiting are rather late manifestations, as is dehydration. Constipation is frequently severe but is occasionally preceded by a short period of diarrhea. A scout roentgenogram of the abdomen may show the enormously dilated loop of torted bowel. The colon proximal to the obstructive lesion may be somewhat distended, but the small bowel as a rule is rather deflated. This is apparently a result of competency of the ileocecal valve and explains why little may be gained by suction with the Miller-Abbott tube. On retrograde barium

study, one may learn the location of the obstruction and possibly also the length of segment involved and the degree of obstruction to the lumen.[1b] However, the barium shadow may merely assume an "ace of spades" appearance at the site of the obstruction.[1c]

It may be difficult to determine just when a grade 3 volvulus of the cecum or sigmoid progresses to the grade 4 stage. Grade 4 is the superimposition of signs and symptoms of peritonitis and blood loss on the grade 3 manifestations. Shock and prostration dominate the picture.

If shock and prostration are superimposed on the picture described in table 3, the process may be considered grade 4.

TREATMENT

Conservative measures appear to be little more than palliative in the management of volvulus of the large bowel. In this problem of altered physiology due to a mechanical derangement, the definitive treatment is as a general rule surgical correction.

In the classification it was brought out that there is a type of volvulus of the cecum or sigmoid which is nonsymptomatic and whose discovery is incidental on roentgen examination. This was classed as grade 1. It would appear to be a rather radical measure to suggest that patients with this type undergo operation; however, it would seem wise to explain the findings and advise the patients that they should seek aid in the event that symptoms do develop.

For grade 2 volvulus of the cecum, there is little to offer as a specific conservative measure because of the inaccessibility of the lesion. Enemas and change of position may be of some aid in assisting in detorsion of the loop, which as yet has not become irreversible. On the other hand, grade 2 volvulus of the sigmoid area is amenable to certain procedures. In addition to rectal clyster, the proctoscope is a great help. A procedure has been described [2b] in which the proctoscope is introduced until the spiral folds of mucosa, caused by the axial torsion, may be seen. After this a long, soft rubber tube can occasionally be made to pass the obstruction under direct vision. If this is accomplished, immediate deflation and detorsion should occur. The tube is then sutured to the perianal skin for a few days. But the treatment should not stop here. At best it is inadequate, as evidenced by a great number of recurrences, and the patient is literally a Damocles with the sword above his head. Much can be said for the procedure, however, in that it may alter the situation sufficiently so that further definitive treatment may be given as an elective procedure rather than an emergency. As soon as the bowel returns to a normal state, which may take one or two weeks, an elective primary resection may be performed.

10. Ritvo, M., and Golden, J. L.: Roentgen Diagnosis of Volvulus of Sigmoid with Obstruction, Am. J. Roentgenol. **56**:480 (Oct.) 1946.

It is felt that patients with grade 2 volvulus of the cecum or sigmoid should be advised to undergo surgical correction, preferably a primary resection and anastomosis. During the quiescent intervals a plication or fixation operation may be performed; however, these procedures have some shortcomings. It is recalled that the patient in case 4 of this series died a year and a half after treatment by detorsion and fixation. One wonders if resection would not have prevented recurrence and death, since the other 4 patients who presented viable bowel at operation and underwent resection are alive today.

The management of grades 3 and 4 volvulus of the cecum and sigmoid is solely a surgical problem. A grade 4 volvulus, by the presence of gangrene, makes exteriorization and resection of the involved segment mandatory. What procedure may best be employed is not so clearcut in cases of grade 3 volvulus. It is apparently the tendency to perform less complete operations in such cases. One must at all times keep the immediate condition of the patient foremost in mind but at the same time not lose sight of the ultimate outcome and subsequent well-being. As a result of increased understanding of intestinal physiology and improved technic and postoperative management, it seems feasible that even in the presence of the obstruction seen in grade 3 volvulus of the large bowel exteriorization resections may be the procedure of choice. This is certainly true for grade 4 volvulus. Such operations as the Paul-Bloch-Mikulicz exteriorization or the Rankin obstructive resection may be employed with relative safety and certainly with the expectancy of curing the volvulus.

There is one additional condition that may cause difficulty. In cases of grade 4 volvulus of the sigmoid the viable distal bowel may be so short as to preclude the possibility of bringing it up to the surface of the abdomen. Two choices of management exist. The end may be closed carefully and dropped back or, if the patient's condition is very grave, a Martel clamp may be employed and the distal blade left in place. The blade should be placed retroperitoneally and the next five to six days used to improve the patient's general condition so that what amounts to a second stage of an abdominoperineal procedure may be carried out.

SUMMARY AND CONCLUSIONS

Volvulus is a term which denotes a twisting or torsion of a segment of intestine. The condition occurs more often in Europe than in this country, the ratio being 40 to 7 per cent. However, the small bowel is involved more frequently in the United States (57 per cent) than in Europe (25 per cent). Even though volvulus of the colon occurs ten times more often in Europe than in this country, the ratio of involvement of the sigmoid to involvement of the cecum is found to be 2:1 in both countries.

Arrests in fetal development are thought to be a significant factor in leading to a predisposition to volvulus of the cecum. Certain predisposing and acquired etiologic factors are brought out in this report.

The pathologic changes are chiefly those of closed loop obstruction and circulatory impairment. The presence of axial torsion is discussed. The causes of distention and the effects of obstruction to venous outflow are reviewed. A mechanical, anatomic and pathologic classification of volvulus of the colon is presented.

Eight cases of volvulus of the large bowel are presented in detail. Three involved the cecum and 5 the sigmoid. An analysis of the findings in these cases is discussed fully. The symptoms of cecal volvulus are those most often associated with low obstruction of the small bowel, while those of volvulus of the sigmoid are for the main part indicative of occlusion of the large bowel.

Volvulus in which gangrene has developed makes exteriorization and resection mandatory. It is suggested that, with the exclusion of cases of nonsymptomatic volvulus, the definite treatment be directed toward resection of the involved segment.

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SOLITARY DIVERTICULUM OF THE CECUM

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IN A RECENT review of the literature Anderson [1] found only 91 cases of solitary diverticulum of the cecum. He collected an additional 8 cases from the Mayo Clinic, which made a total of 99 cases of solitary diverticulum reported in the entire literature. The purpose of this communication is to present 2 new cases recently observed at the Framingham Union Hospital.

REPORT OF CASES

CASE 1.—A 67 year old white married housewife was admitted to the Framingham Union Hospital on Nov. 27, 1947, with the chief complaint of obstipation of three days' duration. During the three months preceding her admission the patient had noted increasing constipation. Increasingly large doses of cathartic were required, and the resulting stools were loose and watery and associated with much flatus. The last bowel movement was three days before admission in spite of repeated enemas and catharsis. There were no other symptoms referable to the gastrointestinal tract. The patient stated that she had never passed blood by rectum although hemorrhoids which had been present for many years had recently become painful. There had been no loss of weight.

The past history was irrelevant. Except for dyspnea on exertion for three years, the review of the systems revealed nothing abnormal.

Physical examination revealed a well developed obese white woman in no distress. The abdomen was tympanitic, soft and nontender, with normal peristaltic sounds. No masses or organs could be felt, and, except for small external hemorrhoids, rectal examination showed no abnormalities.

Laboratory studies were reported on as follows: The urine had a specific gravity of 1.010 and did not contain albumin or sugar. There were 15 to 20 white blood cells and 3 to 5 red blood cells per high power field in the sediment. The red blood cell count was 5,100,000 and the white blood cell count 6,100. The differential count showed 69 per cent polymorphonuclear cells, 28 per cent lymphocytes, 2 per cent monocytes and 1 per cent eosinophils. The hemoglobin content was 16 Gm. per hundred cubic centimeters. The Hinton test of the blood gave a negative reaction. Two specimens of stool gave a positive reaction to the Guiac test for occult blood. The blood sugar level was 128 mg. per hundred cubic centimeters, the total protein 8.4 mg. and the nonprotein nitrogen 49 mg. Phenolsulfonphthalein excretion by the kidneys amounted to 58 per cent in two hours. The

From the Department of Surgery of Boston University School of Medicine and the Surgical Service of the Framingham Union Hospital.

1. Anderson, L.: Acute Diverticulitis of the Cecum, Surgery **22**:479-488 (Sept.) 1947.

electrocardiogram showed evidence of myocardial disease with left axis deviation, low T waves, a slurred QRS complex and low amplitude in lead 4. A roentgenogram of the chest showed slight cardiac enlargement. The pulmonary fields were clear. A roentgenogram of the abdomen showed no evidence of intestinal obstruction.

A roentgenogram made after a barium enema showed the barium to flow readily to the region of the hepatic flexure without evidence of any abnormality. The ascending colon was shortened and narrowed, with a straight and rigid outline.

Roentgenogram of the abdomen after a barium enema showing clover leaf deformity of the cecum.

The narrowing became greater in degree as the cecum was approached, and at its narrowest point, the level of the ileocecal valve, the lumen was about 1 cm. in diameter. On the medial aspect at this level there was a shadow interpreted as an ulcer crater. The cecum showed a deformity resembling a clover leaf (see accompanying figure). There was slight dilatation of the terminal portion of the ileum, and there was tenderness over the region of the cecum and the ascending colon.

A diagnosis of carcinoma of the cecum was made. The patient was prepared for operation with cleansing enemas and administration of succinylsulfathiazole.

On the twelfth hospital day operation was performed under endotracheal cyclopropane anesthesia supplemented with intravenous administration of curare. Exploration through a long incision splitting the right rectus muscle revealed a firm mass 6 inches (15. cm.) in diameter with omentum attached to it by fine fibrous adhesions in the right lower quadrant. The mass was posterior to the cecum and on palpation resembled a neoplasm arising on its posterior wall. It was movable on the posterior abdominal wall and was not attached to the surrounding parietes. The terminal portion of the ileum was normal, and there was no evidence of metastatic carcinoma in the liver or peritoneum. The operative diagnosis was carcinoma of the cecum. A colectomy was performed on the right side, with the removal of 32 cm. of the terminal portion of the ileum, cecum, ascending colon and right half of the transverse colon. An aseptic end to end anastomosis of the ileum to the transverse colon was performed over a three-bladed clamp. A Witzel type ileostomy was then performed 25 cm. proximal to the anastomosis with the use of a size 14 catheter.

Examination of the surgical specimen showed the ileum to be grossly normal. The cecum was surrounded by thick, fatty, lobulated tissue. When the bowel was opened, a diverticulum was found just distal to the ileocecal valve. The opening was round and measured 0.5 cm. in diameter. The diverticulum itself measured 2.2 cm. in width. The mucosa of the diverticulum was normal. The mucosa of the rest of the colon appeared congested but otherwise was normal.

Microscopic examination showed the diverticulum to be of the "true type," with all coats of the intestinal wall present. No inflammatory changes were found. Sections of the ileum and ascending colon failed to reveal significant findings. The dissected regional lymph nodes showed some evidence of chronic inflammatory reaction.

The postoperative course was uneventful until the eighth postoperative day, when symptoms and signs of pulmonary embolism associated with thrombophlebitis in the left calf developed. This responded well to treatment with heparin and dicumarol® (3,3'-methylenebis [4-hydroxycoumarin]). The patient was discharged from the hospital asymptomatic on the twentieth postoperative day. When last examined, nine months after the operation, her bowels were moving regularly and she had no symptoms referable to the gastrointestinal tract.

Case 2.—A 63 year old white married man entered the Framingham Union Hospital on Aug. 26, 1948, with the chief complaint of abdominal pain. A subtotal gastrectomy had been performed two years previously for a benign gastric ulcer. Since then his health had been good until three days before his admission, when pain suddenly developed in the right lower quadrant of the abdomen. The pain was constant and severe and associated with increasing abdominal tenderness. There was no nausea or vomiting, but his appetite had been poor after the onset of the present illness. Since the gastrectomy the stools had been watery, with two or three bowel movements daily. There had been no recent change in bowel habits, no history of bloody or tarry stools and no urinary symptoms.

Physical examination revealed a well developed and well nourished white man. The temperature was 98.2 F., the pulse rate 84 and the blood pressure 160 systolic and 85 diastolic. Pertinent physical findings were limited to the abdomen, which was acutely tender in the right lower quadrant, with maximum tenderness at McBurney's point. Rebound tenderness and muscle spasm were present throughout the lower part of the abdomen but were most marked on the right side. Rectal examination revealed no abnormalities.

Laboratory studies showed the urine to be normal. The red blood cell count was 4,500,000, and the hemoglobin content was 16.8 Gm. per hundred cubic centi-

meters. The white blood cell count was 12,000, and the differential count showed 79 per cent polymorphonuclear cells, 14 per cent lymphocytes and 6 per cent monocytes.

A preoperative diagnosis of acute appendicitis was made. At operation, which was performed under spinal anesthesia soon after the patient's admission to the hospital, the appendix was found to be normal. On the anterior wall of the cecum, 4 cm. distal to the base of the appendix, was a solitary diverticulum 2.5 cm. in its greatest diameter which communicated with the cecum by an ostium 1.5 cm. in diameter. The diverticulum was empty and its ostium patent. The wall of the diverticulum was acutely inflamed and covered with fibrin and appeared gangrenous. Because of the inflammatory thickening, the diverticulum could not be invaginated. Therefore, a rubber-covered clamp was placed across the cecum, and the diverticulum was excised at its neck. The mucosa of the cecum for a radius of 1 to 2 cm. about the neck of the diverticulum was also gangrenous although the muscular and serous layers had a good blood supply. A portion of the gangrenous mucosa of the cecum was excised, and the defect in the anterior wall of the cecum was closed with a double inverting surgical gut suture, reenforced by a layer of silk mattress sutures. The appendix was then removed, and a catheter ileostomy of the Witzel type was performed 15 cm. proximal to the ileocecal valve. A rubber tissue drain was placed to the anterior wall of the cecum. The abdominal wall was closed in layers. The patient tolerated the operation well and was returned to the ward in good condition.

Examination of the excised diverticulum showed it to measure 4 cm. in length and 2.5 cm. in width when opened. Grossly it appeared gangrenous. Examination of the microscopic sections showed such extensive necrotic, hemorrhagic and inflammatory changes that it was impossible to identify the layers that made up its wall, and it could not be determined if it was a "true" or "false" type of diverticulum. The blood vessels showed occlusion of the lumen by thrombotic masses which were loaded with micro-organisms. The appendix was completely fibrosed and showed no evidence of recent inflammation.

The postoperative course was uneventful. Large doses of penicillin were given during the first postoperative week. The ileostomy tube and drain were removed on the seventh postoperative day, after which the bowels moved normally. The patient was afebrile and ambulatory on the fifth postoperative day and left the hospital on the ninth day. He has remained well since his discharge.

COMMENT

Diverticula of the intestinal tract have been classified into two types: congenital or acquired. Congenital diverticula are in general of the "true" type, with walls made up of all the layers of the bowel wall. They usually occur in the small intestine and are most often solitary. Meckel's diverticulum is an example of this type. The acquired diverticula are much more common and usually are of the "false" type, with walls composed only of the mucosal and serosal layers. They are most frequently found in the large intestine and are usually multiple. Noon and Schenk,[2] in their review of 45 cases of cecal diverticula, found 12

2. Noon, Z. B., and Schenk, H. L.: Solitary Diverticulitis of the Cecum, Am. J. Surg. **68**:364-368 (June) 1945.

cases classified as true diverticula and 11 cases as "false" diverticula. The rest were unclassified.

Many theories have been advanced to explain the formation of acquired diverticula, but none is entirely satisfactory. Obesity, constipation, weakness of the bowel wall and increased intracolonic pressure all have been considered etiologic agents. The more frequent occurrence of diverticula in the sigmoid, as compared with the right colon, has led some to believe that the solid consistency of the fecal material in the sigmoid region is a responsible factor.

These various explanations do not apply to the formation of solitary diverticulum of the cecum. Greenfelder and Hilder [3] stated that acquired solitary diverticula of the cecum are sometimes formed from the eversion of a weakened area in the cecal wall between two constricting bands or by the traction of adhesions. In other cases eversion of a weakened area in the cecal wall resulting from the rupture into the cecum of an abscess from an appendical stump may be the etiologic factor.

It is also possible that a solitary diverticulum of the cecum represents a duplicated appendix. In 1941 Waugh [4] collected 14 cases of duplicated appendix from the literature and added a case of his own. In 10 of these cases there were two separate appendixes, although one was usually small and rudimentary. In the other 5 cases the two appendixes were side by side, and both arose from the same site in the cecal wall. Waugh pointed out that according to some embryologists a transient extra appendix does exist at about the sixth week of fetal life and usually atrophies at about the seventh week. A persistence of this extra appendix might explain the occurrence either of a duplicated appendix or of a solitary diverticulum of the cecum. The appendix and cecum can be distinguished from each other by the amount and arrangement of the lymphoid tissue and the presence in the appendix of both the inner circular and the outer longitudinal muscular coats. Theoretically, therefore, if solitary diverticula arise from a duplicated appendix it should be possible to establish this fact from the amount of lymphoid tissue in the submucosa and from the presence of a complete outer longitudinal muscle layer. Practically, however, these criteria fail because the inflammatory process which is usually present or stretching and thinning of the sac distorts the microscopic picture so that it is not possible to recognize these anatomic characteristics.

The clinical picture which accompanies solitary diverticulum of the cecum depends on the presence or absence of inflammation and its severity if present. When the diverticulum is acutely inflamed, the

3. Greensfelder, L. A., and Hilder, R. I.: Cecal Diverticulosis with Special Reference to Traumatic Diverticula, Surg., Gynec. & Obst. **48**:786 (June) 1929.

4. Waugh, T. R.: Appendix Vermiformis Duplex, Arch. Surg. **42**:311-320 (Feb.) 1941.

symptoms and signs are those usually associated with acute appendicitis. There is usually pain and tenderness in the right lower quadrant, with or without vomiting. The temperature is usually under 101 F., and some degree of leukocytosis is often present. A mass may be palpable in the right lower quadrant.

Since appendicitis is the most common lesion involving the right lower quadrant, the most likely preoperative diagnosis will be that of acute appendicitis or appendical abscess. Carcinoma of the cecum, with or without perforation, is the next most common lesion in this region. Other possibilities which may be considered are tuberculosis, actinomycosis and nonspecific ulcers of the cecum which may perforate.

In only 63 cases of Anderson's series was a preoperative diagnosis made, and in 84 per cent of these cases the diagnosis was appendicitis or appendical abscess. A diagnosis of diverticulitis was made in only 6 per cent of the cases. In case 2 of this report a preoperative diagnosis of acute appendicitis was made.

A different clinical picture was presented, as would be expected, in case 1, in which a diverticulum of the cecum without inflammation was present. Constipation was the only complaint, and physical examination of the abdomen showed a normal condition. The lesion was discovered on roentgenographic study of the colon by means of a barium enema, and an incorrect diagnosis of carcinoma of the cecum was made. The problem of exact diagnosis remained unsolved at operation in this case, and the lesion was still considered to be carcinoma at surgical exploration. This is not unusual, however, as shown by the fact that approximately one third of the patients reported on underwent cecectomy or a radical resection of the right side of the colon because the surgeon was unable, at the time of operation, to distinguish between the inflamed diverticulum of the cecum and carcinoma in the absence of demonstrable metastasis.

In about one half of the reported cases either excision of the diverticulum or simple closure was performed, with a mortality of 4 per cent. These are the procedures of choice but are possible only if the amount of pericecal fat and the degree of inflammation permit an accurate operative diagnosis. The mortality rates following resection of the right side of the colon and cecectomy were 11 and 7.1 per cent respectively.[1]

SUMMARY

Two cases of solitary diverticulum of the cecum are described, bringing the total number reported in the literature to 101. One of these cases was unusual in that the only symptom was constipation and pathologically there was no evidence of inflammation. The etiology, diagnosis and treatment are discussed.

DUPLICATION OF THE URETHRA

Report of Two Cases and Summary of the Literature

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DESPITE the rarity of its occurrence, the anomaly of double urethra has long excited interest within the ranks of the medical profession and a rather extensive literature has developed pertaining to the subject. The versatile Aristotle is credited with being the first to make observations from a case of double urethra. Vesalius mentioned Arab writings with descriptions of such malformations. More modern attention begins in the nineteenth century with the published observations of Vidal de Cassis (1834), followed by the reports of Cruveilhier,[1] Jerjavay, Luschka,[2] Lejars [3] and many others. For recent reviews and discussions we are indebted to Fantl,[4] MacKenzie [5] Oudard and Jean,[6] Fronstein and Saigrajeff,[7] Chauvin [8] and Lowsley.[9]

DESCRIPTION OF THE MALFORMATION

An accessory urethra may occur as a complete, second passageway from the bladder to the dorsum of the penis, or it may appear as only a segment of such an accessory pathway on the ventral, or particularly the dorsal, surface of the penis. If only a segment of such a channel is found, it may extend from the bladder out under the symphysis and end blindly, but more commonly it runs from the dorsum of the penis inward and ends blindly. Such accessory urethras, whether complete or incomplete, usually do not have any connection with the normal urethra, but in about one seventh of all cases there is a communication. There are

From the Surgical Service of the Children's Hospital and the Department of Surgery of the Harvard Medical School.

1. Cruveilhier: Traite d'Anat. 1852, p. 614.
2. Luschka: Virchow's Arch. f. path. Anat. **34**:992, 1865.
3. Lejars: Ann. d. mal. d. org. genito-urin. **6**:392, 1888.
4. Fantl, G.: Folia urol. **8**:193, 1913.
5. MacKenzie, D. W.: Surg., Gynec. & Obst. **22**:344, 1916.
6. Oudard, and Jean, G.: J. d'urol. **11**:177, 1921.
7. Fronstein, M., and Saigrajeff: Ztschr. f. urol. Chir. **17**:187, 1925.
8. Chauvin, E.: J. d'urol. **23**:293, 1927.
9. Lowsley, O. S.: New York State J. Med. **39**:1022, 1939.

transitional stages and minor variations of the indicated types, but these hardly justify the intricate classifications which have been set forth by some authors.

In an analysis of the literature, we can summarize the findings in 83 cases of urethral duplication, including 2 of our own which are herein reported. In 48 instances there was a blind, accessory urethra which opened on the dorsum of the penis, ran inward for a variable distance of one to several centimeters and did not in any way connect with the urinary tract. There were at least three other reports of a blind accessory canal on the ventral surface of the penis. There were 12 cases in which some sort of a tract opened on the dorsum of the penis, ran through the substance of the penis and communicated with the normally situated urethra. In 1 case an accessory urethra left the bladder, coursed through the substance of the penis and emptied into the normal urethra within the glans. Finally, in 19 cases there was a second urethra which arose independently from the bladder and which coursed forward to open on some part of the dorsal side of the penis, an example of which is depicted in figures 2 and 3.

Descriptions of the blind, accessory urethras have been gathered from the following reports: From the composite surveys by Fantl, MacKenzie, Fronstein and Saigrajeff and Lowsley there were 44 cases up to 1939. Since then 7 additional cases have been described, including 1 of our own. O'Herron and Webster [10] contributed 2 cases, while Haslinger,[11] Rinker,[12] Fong [13] and Irmisch and Cook [14] each described 1.

While most of the dorsal blind pouches open externally, there are two descriptions which are of particular interest in showing more extensive developmental aberrations. Meisels [15] noted an accessory penile opening in a 27 year old man; this opening led into an accessory canal which was patent for 12 cm. and the blind end of which was connected with the bladder by a fine thread of tissue. Pribram [16] described a somewhat similar finding in a 64 year old man in whom the accessory urethral orifice opened 3.5 cm. behind the corona of the penis and the tract extended inward for a distance of 4 cm. At autopsy a funnel-shaped retraction was discovered in the anterior wall of the bladder 2 cm. above the vesical orifice of the normal urethra; this outpocketing was about 2 cm. deep and extended in a direction toward, but did not communicate with, the blind end of the accessory urethra.

10. O'Herron, M. D., and Webster, F. A.: J. Urol. **55**:391, 1946.
11. Haslinger, K.: Ztschr. f. urol. chir. **33**:24, 1939.
12. Rinker, J. R.: J. Urol. **50**:331, 1943.
13. Fong, E. E.: Radiology **46**:380, 1946.
14. Irmisch, G. W., and Cook, E. N.: Minnesota Med. **29**:299, 1946.
15. Meisels, V.: Pest. med.-chir. Presse, Budapest **29**:585, 1893.
16. Pribram: Praeger Vierteljahrsschr. **4**:44, 1867.

Cases of Complete Double Urethra

Author	Age	Clinical Picture	Method of Diagnosis	Treatment
Stockmann: Monatsbericht d. Krankheiten des Sexualapparates, 1897, P. 474	24	Accessory opening dorsally in balanopreputial groove of glans; gonorrhea in both tracts; minimal incontinence	Catheters into bladder through both openings did not touch; no interurethral communication seen with urethroscope	Gonorrhea treated; no operation
Rona: Deutsche med. Wchnschr. **21**: 831, 1905	6	Dorsal groove on glans and shaft of penis led to accessory opening; incontinence	Catheters into bladder with urine through both; sounds into bladder did not touch	Surgical excision
Broca: Soc. de Chir. de Paris, 11 decembre, 1912	Child	Accessory opening dorsally in balanopreputial groove with dorsal groove on glans; two streams on urination but no incontinence	Roentgenograms of catheters in both tracts without touching one another	No operation
Fronstein: J. d'urol. **4**: 714, 1913.....	23	Accessory opening dorsally on glans; two streams occasionally; no incontinence	Metal sounds into bladder through both tracts did not meet; cystoscopy and use of colored dyes	No operation
Lebrun: J. d'urol. **4**: 35, 1913; **2**: 381, 1912	20	Accessory opening dorsally at base of penis; dorsal groove on penis from glans to opening; incontinence	Catheters and bougies passed through both openings into bladder	Surgical excision
Lissowskaja: Zentralbl. f. d. ges. Chir. **5**: 381, 1914	36	Accessory opening dorsally at base of penis; mild incontinence	Surgical exploration; accessory tract went over symphysis to enter bladder	Surgical excision
Ritter: Ztschr. f. urol. Chir. **20**: 5, 1926	2½	Accessory opening dorsally in balanopreputial groove with dorsal groove on glans; incontinence	Roentgenograms with catheters through both tracts into bladder	Surgical excision
Perlmann: Ztschr. f. urol. **24**: 508, 1930	34	Accessory opening dorsally at base of penis; short groove leading to opening; two urinary streams; no incontinence	Cystoscopic view of catheter entering bladder via accessory tract	No operation
Nicoletti: Gior. ital. dermat. e. sif. **72**: 1026, 1931	20	Accessory opening dorsally on glans; gonorrhea in accessory urethra only; no incontinence	Urethrograms and use of colored dyes indicated complete double urethra	Gonorrhea treated; no operation
Heymann: Ztschr. f. urol. Chir. **38**: 290, 1933	27	Accessory opening dorsally in balanopreputial groove with dorsal groove on glans; gonorrhea in both tracts; no incontinence	Urethrograms and colored dyes confirm diagnosis	Gonorrhea treated; no operation
Delvigne: Ann. Soc. méd.-chir. de Liége **4**: 193, 1934	12	Accessory opening dorsally in balanopreputial groove with dorsal groove on glans; two streams on urination but no incontinence	Catheterizations and roentgenograms with metallic sounds through both tracts into bladder	No operation
DiBenedetti: Soc. ital. di urol., Milano, April 19, 1935 (cited by Astuni)	..	Complete double urethra		
Fuchs: Urologia **2**: 249, 1935.....	60	Accessory opening dorsally on glans; two urinary streams; no incontinence	Urethrograms; interpretation equivocal; no further studies	No mention of operation
Astuni: Urologia **4**: 32, 1937.....	18	Accessory opening dorsally in balanopreputial groove with dorsal groove on glans; no incontinence	Urethrograms and catheterizations with use of colored dyes	No operation
Haslinger [11]	20	Accessory opening dorsally in balanopreputial groove with dorsal groove on glans; abnormal dorsal angle of penis; no incontinence	Catheterizations; cystoscopic view, catheter entering bladder via accessory tract; urethrograms; cystogram showed apparent septum dividing bladder	No operation
Bernan: Bol. y. trab. Soc. de cir. de Córdoba **3**: 339, 1942	..	Complete double urethra		
Irmisch and Cook [14].....	45	Accessory opening dorsally on glans associated with suggestive partial diphallus; double stream; no incontinence	Cystoscopic view of vesical orifice of accessory tract	No operation
Moore, C. B.: J. Urol. **56**: 130, 1946.....	24	Accessory opening dorsally in balanopreputial groove with dorsal grodve on glans; minimal incontinence	Urethrograms on voiding; one and then the other orifice occluded	No operation
Gross and Moore (1949).....	7	Accessory opening dorsally near base of penis; dorsal groove on shaft; rudimentary accessory glans; incontinence	Catheterizations with use of colored dyes; urethrograms	Surgical excision

While the vast majority of accessory urethras are on the upper surface of the penis, a few were found on the ventral surface of the organ, but none of the latter ever connected with the bladder, regardless of the length of the tract. Von Dittel [17] and Lenartowicz [18] reported examples of blind-ending, rather short accessory, canals of this sort. In Rinker's [12] case, in which the ventral accessory tract was longer than in any to be found in the literature, the canal ran upward between the bladder and the rectum, terminating blindly just below the right iliac vessels. It required three operative procedures (penile, perineal and transabdominal) to remove it completely, and at no time was a communication found between the anomalous structure and the bladder or the normal urethra.

Regarding the twelve accessory urethras which did not open into the bladder but which did join the normal urethra, the following descriptions are available. In 1916 MacKenzie collected 7 cases and added 1 of his own. Since then 4 additional cases have been reported by Bernadet,[19] Fronstein and Saigrajeff,[7] Pytel [20] and Bonanome.[21]

We have been unable to find a complete summary or a satisfactory analysis of the available information regarding cases of complete double urethra which communicate with the bladder and hence we wish to list herewith in table form the findings which have been gleaned from the literature, adding a case of our own. In an analysis of the 19 cases, it is evident that the accessory urethral tract is situated above, or dorsal to, the normal urethra in all instances. In all but 1 the accessory tract passed under the symphysis to join the bladder. In 4 patients the distal orifice of the accessory tract was located on the glans, in 8 it was in the balanopreputial groove and in 6 it was situated at the base of the penis; in only 1 case was the external orifice in the midportion of the shaft of the penis. In all instances, except those in which the external orifice is on the glans, there is an epispadias-like groove on the shaft of the penis leading down to the external orifice of the accessory tract. In 2 of the cases there has been a rudimentary diphallus associated with the anomaly. In the rare condition reported by Haslinger a thin septum divided the bladder into two compartments.

From the present discussion we have excluded (1) examples of accessory tracts which have resulted from trauma or infection, (2) cases in which there is an imperforate anus associated with a rectal fistula opening ventrally on the shaft of the penis and (3) those rare instances of anomalous ejaculatory ducts which open on the dorsum of the penis. In the last category is the case of Luschka in which the orifice of the

17. von Dittel: Wien. med. Wchnschr. **39**:395, 1869.
18. Lenartowicz, J. T.: Dermat. Wchnschr. **56**:97, 1913.
19. Bernadet, G.: Bull. de méd., Paris **37**:1162, 1923.
20. Pytel, A.: Urol. & Cutan. Rev. **39**:23, 1935.
21. Bonanome, L.: Arch. ital. urol. **19**:361, 1942.

accessory canal was at the base of the penis, the canal being 1.5 cm. in length and apparently derived from the confluence of four excretory ducts of what appeared to be an aberrant prostatic lobe. In the same class would be the case of Cruveilhier, in which autopsy showed two ejaculatory ducts passing dorsally, without entering the prostate, to join each other and to form an independent accessory seminiferous canal which opened on the glans dorsal into the normal urethral opening.

CLINICAL SIGNIFICANCE

In many cases of double urethra of the various types there are no important symptoms referable to the anomaly. For this reason we could assume that the frequency with which this malformation appears is probably greater than is indicated by the number of cases which have actually been recorded.

When symptoms arise, double urethras have often been found to be the site of gonorrheal infection. In only a small number of the cases has infection been of a nonspecific type. It is apparent that, with adequate exposure, gonorrhea is more easily acquired in an accessory tract than in a normal urethra and that, once acquired, it is more resistant to treatment. This is presumably due to poor drainage and the absence of a cleansing urinary stream in the accessory tract in most cases. In his excellent review of 44 cases of blind-ending accessory penile tract, ventral as well as dorsal, Lowsley reported that gonorrhea was present in 26. In 15 the infection was in the accessory tract only, while in 8 it was in both the normal and the anomalous passages. Gonorrhea was found only in the normal urethra in 3 cases.

Patients with blind-ending double urethras rarely seek medical attention for symptoms other than those due to infection, gonorrheal or otherwise. In rare circumstances one may find symptoms of urinary obstruction, which result from accumulation of material in the blind-ending tract which gives pressure on the normal urethra.

In cases in which the accessory tract communicates with the normal urethra the patient is commonly troubled by the presence of a double stream during urination. There is, however, no incontinence in this type of anomaly.

Whenever two complete urethras emerge from a bladder, it is interesting to note that disturbance of urinary control is much less frequently encountered than one might be led to expect from the nature of the condition. Even in the 7 cases in which incontinence was the predominant symptom, it usually occurred only under conditions of stress, excitement or overdistention of the bladder. Hence, in some cases it must be postulated that both the normal and the accessory urethra are under the influence of a common sphincter mechanism at the bladder outlet. In 5 patients there was a disturbing double urinary stream but

no incontinence. In 3 cases gonorrheal infection was the main complaint. Two of the patients with complete double urethra were bothered by an abnormally dorsal position of the penis during its resting state. The accessory urethra apparently acts as a bow-string because of its attachment to the bladder or the under surface of the pubes. The angle on erection is also exaggerated because of the same mechanism. A small number of patients have desired surgical correction of this deformity for cosmetic reasons.

The methods of studying and classifying each case of urethral anomaly fall into the category of relatively simple and fundamental urologic maneuvers. Judicious probing and sounding often give useful information. The use of colored dyes may be helpful in determining the patency of the accessory tract. If the dye instilled into the accessory tract appears in the normal urethra or bladder, an intercommunication obviously exists. The point of connection can often be located by cystoscopic or urethroscopic view of the area at which the dye enters the normal urinary tract. If the caliber of an accessory tract is sufficiently great, a catheter or bougie may be inserted in it and the union with the normal tract may be seen on urethroscopic or cystoscopic examination.

Roentgenologic examination of the normal and accessory tracts using radiopaque solutions, radiopaque catheters or a combination of both often gives important data. Roentgenograms may be taken either on instillation of the radiopaque solution or on subsequent voiding. It is sometimes helpful to obtain serial roentgenograms on the occlusion of one and then the other orifice during voiding of the radiopaque material.

Other studies should include cultures if infection is present. Because of the possibility of associated anomalies of the upper urinary tract, investigation by means of intravenous or retrograde pyelograms may be indicated, particularly if other symptoms are present which would suggest a pathologic process in the ureters or kidneys.

TREATMENT

In the management and treatment of patients with some form of double urethra, we feel that no therapy is indicated for the majority who are asymptomatic. Whenever there are important complaints, it is possible to employ surgical measures, chemotherapy or sometimes a combination of the two, depending on the nature of the complication.

When there is gonorrheal infection, penicillin provides the treatment of choice. The drug should be given parenterally or orally, but in addition it should be instilled locally into the accessory tract. The overall results in this form of therapy have been satisfactory. Surgical intervention may occasionally be indicated in certain cases in which chemotherapeutic attack alone fails.

Of the patients with a simple blind urethral pouch or tunnel, probably only a third will require operation for one reason or another. In about half of the operations which have been performed, the entire structure has been dissected out, while in the remaining ones the tract was merely incised so that it could be laid open for curettage of its epithelial lining. It is our impression that such incision, marsupialization and curettage give results which are distinctly inferior to those which are obtained by complete excision. Furthermore, we feel that it is unwise to attempt to unite normal and accessory tracts by longitudinally cutting down the septum of tissue between them. O'Herron and Webster reported an unsatisfactory result after employment of this operation, stating that the urinary stream subsequently had a dispersed or "nozzle" effect.

Surgical intervention may be indicated in rarer cases in which the anomaly is sufficiently deforming to warrant it for cosmetic reasons. When there is a cleft of the foreskin, an unsightly dorsal groove, an accessory penis or other deformity, much can be accomplished by the performance of proper plastic procedures.

Operation is certainly in order for those patients who have a complete accessory urethra which is accompanied with urinary incontinence or with the disturbing phenomenon of a double urinary stream. Furthermore, a certain number of these patients have bothersome dorsal angulation of the penis, for which excision of the taut, superior, accessory urethra should be advised. Dissection and removal of the entire tract is not difficult; the progressive steps in such an undertaking are clearly indicated in figures 4 and 5 and need not be described here in further detail. Needless to say, a meticulous dissection will produce the least local trauma and subsequent scarring. Furthermore, use of the finest suture materials in repair of the subcutaneous tissues and skin of the penis will lead to the best cosmetic result. It is probably advisable to avoid long, continuous, midline incisions which run along the dorsum of a penis and up over the lower part of the abdomen, for fear that any subsequent contraction of such a scar might lead to undesirable dorsal angulation of the penis. As is shown in figures 4 *B* and *E*, a more suitable operative approach consists in making a transverse wound just below the pubes (which permits adequate exposure beneath the symphysis), joining this with a longitudinal incision along the shaft of the penis and making an entirely separate opening for the suprapubic cystotomy. This leaving of a zone of normal skin between the suprapubic incision and the penile incision will minimize any tendency to dorsal penile displacement from contractures of the wound. The total excision of the entire accessory urethral tract in our second patient—as shown in figures 4 and 5—produced complete urinary continence and also a highly satisfactory cosmetic result.

REPORT OF CASES

CASE 1.—*Blind-Ending Dorsal Accessory Urethra.*—M. R., a 5 year old boy, was admitted to the hospital in January 1945 for elective repair of an indirect inguinal hernia on the left side. On physical examination, a small accessory opening on the superior aspect of the glans penis was discovered (fig. 1). It had always been completely asymptomatic and had never discharged material of any sort. This opening admitted a probe for a distance of approximately 5 cm. and appeared to end blindly. No discharge, urinary or otherwise, was noted. Urethrograms showed no abnormality of the bladder contour or of the normal urethra. Radiopaque material was injected into the accessory dorsal urethral tract and suitable exposures were made. The tract was about 5 cm. in length, ran along the dorsum of the penis and ended blindly below the pubic bone, where it had a tiny, bulbous,

Fig. 1.—Photograph showing the blind accessory urethra on the dorsum of the penis in case 1.

irregular enlargement. The hernia was repaired satisfactorily, and the postoperative course was uneventful. It was felt that no surgical procedure was needed for the dormant accessory urethra. The patient was last seen in August 1948, at which time the accessory urethra was still asymptomatic. There was no discharge of any kind from this sinus.

CASE 2.—*Complete Double Urethra.*—M. E., a 7 year old boy, was admitted to the hospital in May 1948 because of deformity of the penis. He weighed 4 pounds (1.8 Kg.) at birth. The family history was noncontributory. Growth and general development had been normal. There was no history of serious illness.

At birth the child was noted to have an abnormality of the penis, with a second opening on its upper surface. He had always been able to void without hesitation

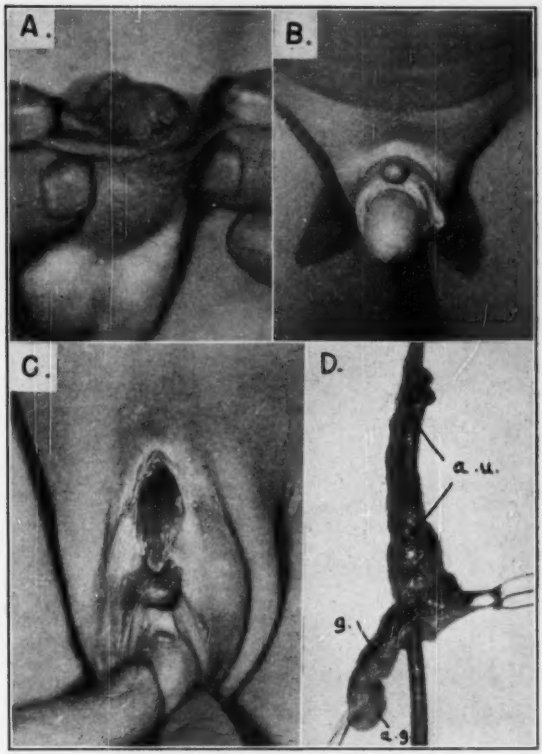

Fig. 2.—Photographs of double urethra in case 2. *A*, under side of penis showing normal urethral orifice. *B*, superior view of penis showing small accessory glans. *C*, penis held down, showing accessory glans, groove along dorsum of penis and orifice of accessory urethra at base of penis. *D*, the excised tract; *a.g.* indicates accessory glans, *g* groove from dorsum of penis and *a. u.* accessory urethra.

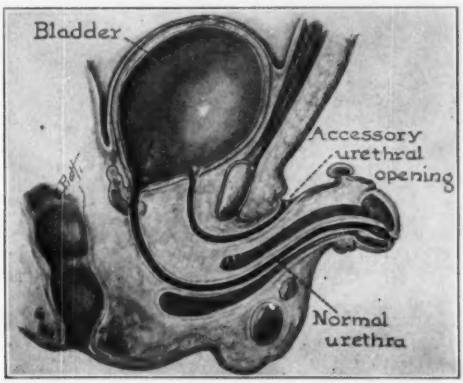

Fig. 3.—Saggital sketch of structures in second case here reported. The inferior urethra is normal in every way and communicates properly with the bladder at its trigone. The accessory urethra emerges from the bladder anterior to its sphincters, courses just beneath the pubic bone and opens on the dorsum of the penis.

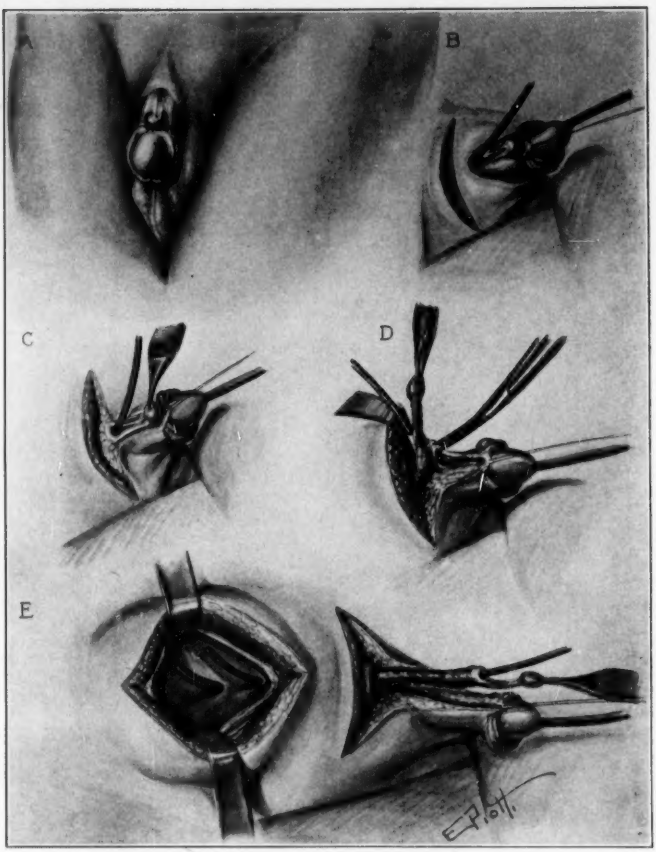

Fig. 4.—Steps in operative removal of accessory urethra. *A*, sketch of the penis, showing the long dorsal trough, with a small accessory glans at its apex and the urethral opening at its base. *B*, catheters inserted into both urethras. Transverse incision just below pubic bone. *C*, dorsal trough and accessory glans freed from surrounding tissue. *D*, accessory urethra being freed at base of penis and under pubes. *E*, suprapubic cystotomy, showing catheters projecting into bladder. The larger catheter comes through the normal urethra which connects with the bladder at the apex of the trigone. The smaller catheter lies in the accessory urethra.

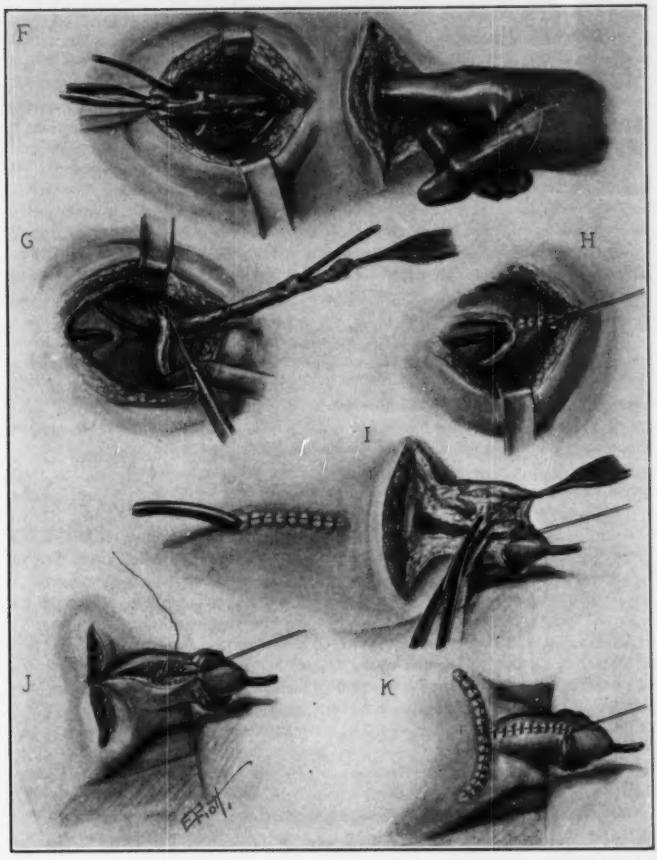

Fig. 5.—Operative steps continued. *F*, freed accessory urethra is threaded upward under symphysis pubis and is pulled up anterior to the bladder. *G*, accessory urethra being severed from the bladder. *H*, closure of the accessory opening in the bladder. *I*, suprapubic wound closed, mushroom catheter in place. Dissection of skin flaps from sides of penis. *J*, closure of subcutaneous tissue on dorsum of penis. *K*, penile reconstruction completed.

through a normally placed urethra and had a good urinary stream. The opening on the top of the penis occasionally leaked urine, this usually occurring during periods of coughing, excitement or exercise. Relatively small amounts of urine escaped from the dorsal opening, but these were sufficient to soil his clothes.

Physical examination was essentially noncontributory except for the penile anomalies. The general size and contour of the penis were normal for a boy of this age (fig. 2). On the under surface of the organ was a urethra normally situated at the apex of the glans, which could be palpated and could be probed through a meatus and in every way appeared to be normal. On the dorsum of the penis, and located at the balanopreputial fold, there was an accessory mass 6 to 7 mm. in diameter, which was irregular in shape and had the consistency and appearance of a rudimentary glans. Running proximal to this, along the shaft of the penis, was an open groovelike trough lined by a reddened membrane, and at the proximal end of this (near the base of the penis) the accessory urethra opened. When the patient voided, there was an excellent stream of urine from the normal ventral urethra and a small escape of urine from the accessory urethral opening. Catheters could easily be passed through both of the urethras into the bladder, and urine flowed through each catheter.

Routine examinations of the blood and urine showed them to be normal. Intravenous pyelograms revealed no abnormalities. Cystograms were made with catheters in both of the urethral tracts. The ventral one followed a completely normal course into the bladder. The accessory tract ran beneath the symphysis pubis and then entered the bladder at a point at least 3 cm. anterior to the normal outlet. The anatomic arrangements are shown in figure 3.

Because of the urinary incontinence, which often led to wetting of the boy's clothes, and because of the unusual appearance of the penis, surgical intervention was advised. Various steps in this procedure are shown in figures 4 and 5. Under ether anesthesia, catheters were inserted into the bladder through both urethral tracts. Blue dye injected through one catheter immediately flowed back through the other one. An incision was made around the accessory glans and the epispadias-like groove on the dorsum of the penis, these structures being cut away from the penis and the separation carried down toward the root of the organ where the accessory urethra was met and along which the dissection was continued. To gain adequate exposure in the depths of the wound below the pubic bone, a transverse cutaneous incision was added, which greatly facilitated the freeing of the accessory tract from beneath the symphysis. A midline suprapubic incision was now made, and the bladder was opened. The two catheters could be seen entering the bladder through separate openings. The normal urethra joined the bladder in a proper position on the trigone, while the accessory urethra connected with the bladder about 3 cm. in front of this. Dissection was carried down in front of the bladder, and the accessory urethral tract was identified and freed except for its attachment to the bladder. At this stage, the distal part of the accessory tract (which had been previously liberated) was threaded back under the symphysis and was brought out through the suprapubic wound. The entire accessory urethral tract was then cut off from the bladder, after which the defect in the bladder wall was repaired by infolding it with interrupted chromic surgical gut sutures, reenforced externally by a layer of silk stitches. A mushroom catheter was placed in the bladder, and the cystotomy opening was closed with a running, inverting suture of surgical gut supplemented by an additional, inverting layer to the muscularis. The superficial layers of the suprapubic wound were now appropriately closed. The penis was repaired by widely undermining the dorsal and lateral portions of the foreskin, this tissue being allowed to slide toward the base and the dorsum of the

penis. Subcutaneous tissues were brought together with interrupted fine silk sutures, and the skin was approximated with fine silks.

Postoperatively, the bladder was continuously drained by the urethral and the suprapubic catheters, which were left in place for twelve days. The patient received sulfadiazine and penicillin throughout his postoperative course in the hospital. Packs saturated with magnesium sulfate were applied to the penis to minimize any swelling. The wounds healed well, and the sutures were removed on the tenth postoperative day. The suprapubic fistula closed readily, and the patient was discharged home in good condition on the fourteenth day. The cosmetic result has been excellent; the urinary control is perfect.

SUMMARY

Accessory urethras may appear on the ventral surface of the penis, but much more commonly they are found on the dorsal aspect of the organ. Observations from 83 cases are collected and summarized. In about two thirds of them blind pouches are present which extend for several centimeters in a direction toward the bladder; in rare instances they extend from the bladder outward and end blindly. About one sixth of the patients have a short dorsal tract, which communicates through the substance of the penis with a normally placed urethra. In about one quarter of the cases there is a complete, accessory urethra, which lies cephalad to the normal urethra and which forms a second excretory tract leading out from the bladder to some part of the penis.

Blind urethral pouches have most commonly been brought to the attention of physicians because of a superimposed infection, most often gonorrheal in nature, which may be difficult to eradicate because there is no urinary stream to flush out the pocket. However, chemotherapy has generally been effective in curing such infection, though in some instances this has had to be combined with surgical removal of the tract.

When an accessory urethra consists of a dorsal, epispadias-like groove or when it is accompanied with a second rudimentary glans, plastic correction is worth while from the cosmetic viewpoint.

Nineteen cases are summarized in which the accessory urethra has been complete and has formed a second passageway from the bladder. Such a malformation is apt to be troublesome because of formation of a double urinary stream or because it may be accompanied with incontinence whenever the accessory tract lacks a sphincteric mechanism at the outlet of the bladder. If such complaints arise, it is possible to excise the entire accessory tract, with excellent cosmetic and functional results.

EFFECT OF VARIATIONS IN THE AMOUNT OF MERCURY ON THE SPEED OF INTESTINAL INTUBATION

MEYER O. CANTOR, M.D.
DETROIT

IN RECENT years the widespread acceptance of metallic mercury within the head of tubes for intestinal decompression as a highly effective method of obtaining intestinal intubation has resulted in its use in practically all such tubes. It was found by using metallic mercury in the balloon of these tubes that the number of successful intubations increased and the duodenum was intubated more rapidly. The amount of mercury which various authors advocated to be used ranged from 3 to 10 cc.[1] As a result of the observations of my colleagues and me over the past three years, during which time 441 patients were intubated, we attempted to make certain observations and conclusions regarding the optimum amount of mercury that should be used in any type of case.

In 1589 Galileo demonstrated that bodies of different weights fell with the same velocity. He proved this important point by the simple expedient of dropping masses of different weights from the top of the leaning tower of Pisa and furnished to the onlookers undoubted proof of this idea. Unfortunately the demonstration of the speed of descent of intestinal tubes does not lend itself in vivo to such classic demonstration. If the length of time required for an intestinal tube to pass from the external nares to the lower reaches of the intestinal tract is considered as the speed of descent and it is remembered that in its passage the tube must traverse both the cardiac and the pyloric sphincters as well as various flexures, it should be obvious that other factors must be brought into play aside from the effect of gravity on a free-falling mass. Lake's [2] demonstration that increasing the weight of the head of metallic-tipped gastroduodenal tubes did not increase appreciably either the speed of gastroduodenal intubation or the percentage of successes would tend to suggest that Galileo's original concept was also true when applied to gastroduodenal intubation. By using metallic mercury, whose

From Grace Hospital.

1. Wild, J. J.: Apparatus for Intestinal Intubation, Brit. M. J. **1**:815 (June 17) 1944. Harris, F. I.: New Rapid Method of Intubation with Miller-Abbott Tube, J. A. M. A. **125**:784 (July 15) 1944. Cantor, M. O.: Mercury: Its Role in Intestinal Decompression Tubes, Am. J. Surg. **73**:690 (June) 1947.

2. Lake, M.: The Influence of the Weight of the Duodenal Tube Tip on its Entrance Time, Am. J. Digest. Dis. **7**:136 (March) 1940.

cohesive power and mobility are highly important physical properties, we attempted to review our cases in an effort to determine whether varying the amount of mercury within the balloon of the tube would increase the speed of descent or the percentage of successful intubations.

When deciding just how much mercury to use within the balloon of the intestinal tube as a propulsive mechanism, we were able to divide all patients being intubated into four main groups. We began our study by using 5 cc. of mercury within the balloon and standardizing our procedure of intubation so that the same technic was used in all cases. We felt that in this way differences in the speed of descent or the success of intubation could not be ascribed to any one technic. The variation would of necessity be due either to the propulsive mechanism, in this case the amount of mercury used in the balloon, or to differences as a result of the type of patient being intubated. In regard to the latter consideration, we should be able to find out whether certain types of intestinal distention require more or less mercury as a propulsive mechanism.

CLASSIFICATION OF PATIENTS

Group 1.—This group was found to consist of all patients in whom there had been no loss of tone in the gastrointestinal tract or no impairment of peristaltic activity due to muscular weakness. In this group were found patients with mechanical obstruction of the bowel from whatever cause seen relatively early in the course of the disease and before a paralytic ileus ensued. It was found to matter little whether the cause of the obstruction was adhesive bands or carcinoma of the sigmoid. As long as peristaltic activity was present and could be heard, the patients were considered as falling in this group. We found that for these patients 4 to 5 cc. of metallic mercury within the balloon of the tube was sufficient to carry the tube into the midjejunum within twenty-four hours. In many patients in whom the intestinal tube was inserted prior to resection of the bowel for nonobstructing lesions, the head of the tube would be demonstrated in the ileum at the end of twenty-four hours. In such cases intubation was found to be easy and the incidence of failures was less than 4 per cent. In many instances failure was turned into success by a change in the technic of intubation. Roentgenograms taken twenty-four hours after intubation generally demonstrate that the usual finding in this group is the presence of the tube head at the midjejunum. The pattern assumed by the tube, however, is different in each case. Roentgenograms of the same patients taken forty-eight hours after intubation reveal the head to be in the ileum. These patients were all ambulatory. Figure 1 *A* is a roentgenogram of a patient classified in this group. This roentgenogram was taken twenty-four hours after intubation. Note the position of the tube head far down the gastro-

intestinal tract. We thought that some difficulty would be encountered in intubation of this patient. Because of this, 8 cc. of mercury was used. With the permission of the patient and after the first tube was in place, we passed a second tube through the other nostril, using only 4 cc. of mercury in the balloon. Twenty-four hours later a roentgenogram was taken, as shown in figure 1 *B*. Note that the second tube, containing only one-half the amount of mercury in the first tube, proceeded down the gastrointestinal tract with the same speed as the first. This suggests that for intubation of patients in this group 4 to 5 cc. of mercury as a propulsive agent is just as effective as 8 cc. This same experiment was repeated on other occasions, with exactly the same results. We attempted

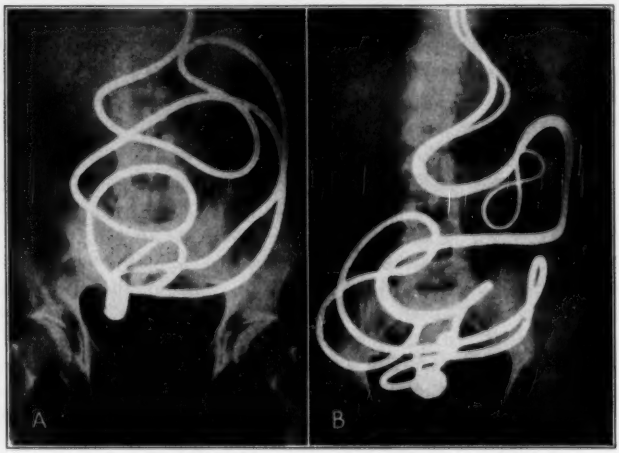

Fig. 1.—*A*, roentgenogram of a patient, a Negro aged 46, with uremia. Note the position of the tube head containing 8 cc. of mercury at the end of twenty-four hours. *B*, same patient as in *A*, in whom a second tube was passed with 4 cc. of mercury in the head. Note that twenty-four hours after passage of the second tube both tube heads are at approximately the same distance along the gastrointestinal tract.

on many occasions to increase the speed of intubation by increasing the amount of mercury to 9 cc. Invariably the tube head would be found in approximately the same position in the gastrointestinal tract whether 5 or 9 cc. of mercury was used.

On four occasions one-half the amount of mercury leaked out of the balloon, which left 2 cc. available for propulsion. A roentgenogram taken forty-eight hours after intubation when this happens invariably shows that the tube head may reach the duodenojejunal flexure in this period. Looping of the tube in the second and third portions of the

duodenum because of the slowness of descent of the balloon containing only 2 cc. of mercury is not unusual. From these observations, we were led to the conclusion that in intubation of patients with no impairment in intestinal tonus or peristaltic activity 4 to 5 cc. of mercury was the optimum amount to be used in the balloon as a propulsive agent.

Group 2.—This group consisted of all patients who were high-strung and nervous. The reason for intubation was found to make little difference in the group when the decision as to how much mercury to use was made. The vast majority of the patients had either cardiospasm or pylorospasm, with the result that the tube for intestinal decompression was trapped in the lower end of the esophagus or in the stomach. As long as the cardiac or pyloric sphincters remained in spasm, the tube would not pass if 4 to 5 cc. of mercury were used in the balloon. Such patients were always apprehensive and greatly feared intubation. The intubator was immediately informed by the patient or found out for himself as soon as the tube head was inserted into the nose that he was dealing with a patient in this group.

The use of 4 to 5 cc. of mercury in the balloon of intestinal tubes passed in patients in this group was found to delay a successful intubation unnecessarily. In 7 patients the tube failed to pass. Figure 2 *A* is a roentgenogram of a patient in this group for whom 5 cc. of mercury was used in the balloon. Note that the tube head was trapped in the lower end of the esophagus. The tube was then removed and 9 cc. placed in the balloon and the same technic of intubation used. Figure 2 *B* is a roentgenogram taken twenty-four hours after passage of the second tube. In 7 cases the same procedure of increasing the amount of mercury used to 8 or 9 cc. resulted in successful intubation after failure had occurred with the use of 4 cc.

In intubating patients in this group, we have usually found it necessary to use from 8 to 10 cc. of mercury within the balloon. This amount of mercury will generally by-pass any spastic sphincter if the tube head is permitted to press on it. In a case of cardiac sphincter, ambulating the patient or standing him up results in the weight of one fourth of a pound (9 cc.) of cohesive labile heavy metal (mercury) pushing on the cardiac sphincter. The lability of the mercury and its cohesive power are such that successful passage through the cardiac sphincter is generally obtained in this fashion. If the pyloric sphincter is in spasm, then the position in which the patient is placed depends on the type of stomach being intubated. In the case of a steerhorn stomach with a low-lying pylorus, ambulation and motion of the patient result in the tube head pressing on the most dependent portion of the stomach, which in this instance would be the pylorus. If the stomach is of the J type, then it is important that the patient be turned on the right side and inclined obliquely face downward in addition to elevating the foot of the bed

from 12 to 15 inches (30 to 38 cm.). In this position, the first portion of the duodenum becomes downhill and the pylorus becomes the lowest point in the stomach.

From our observations it would seem that in intubating patients who are nervous and apprehensive and in whom sphincteric spasm might be anticipated the percentage of failures would be materially reduced by the use of 8 to 9 cc. of mercury within the balloon of the tube.

Group 3.—All the patients in this group presented one thing in common, that is, atony of the gastrointestinal musculature or loss of the coordinated intestinal movement necessary to propel an intestinal tube downward. This condition is clinically classified as atonic ileus if no

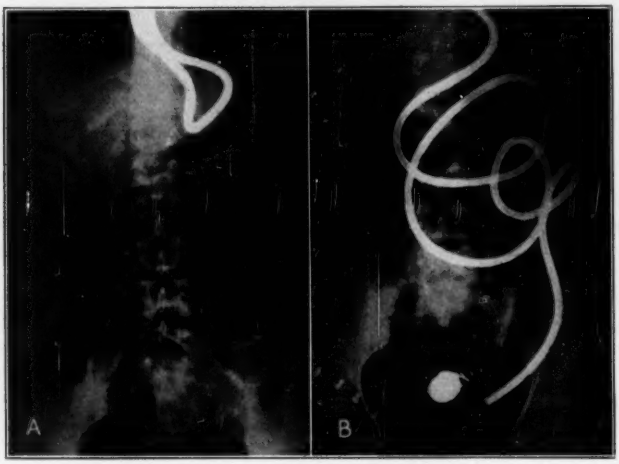

Fig. 2.—*A*, roentgenogram of a white woman aged 40 with a diagnosis of ruptured appendix. The patient was nervous and apprehensive. Note the tube head containing 5 cc. of mercury trapped in the lower end of the esophagus because of cardiospasm. *B*, roentgenogram taken twenty-four hours after 9 cc. of mercury was placed in tube head and the patient ambulated.

specific source is found in old debilitated persons or as paralytic ileus when found in patients with peritoneal infection or postoperatively. Such patients are usually described by clinicians as having "a silent abdomen" because no peristaltic sounds are audible. We have found it imperative to increase the amount of mercury used in the tube head to 8 or 9 cc. for successful intubation in a higher percentage of them. In addition, these patients must be so maneuvered that the area into which the heavily weighted tube head is to go will always be downhill. With the use of such amounts of mercury in an atonic or paralytic gastrointestinal tract,

it is essential to ambulate the patient when the tube head has passed through the third portion of the duodenum. In such patients little help is given by peristaltic activity and the most dependence is placed on the effect of motion and the positioning of the patient on the weighted tube head, which always seeks the most dependent level. By the use of 4 to 5 cc. of mercury, many tubes will be successfully passed in patients in this group, but the percentage of failures will be high. Since it is in this type of patient that intestinal intubation is so important, it becomes highly desirable to pass a tube as rapidly as possible. In 15 patients in this group the use of 5 cc. of mercury within the balloon of the tube head resulted in a failure to intubate in twenty-four hours. When the tubes

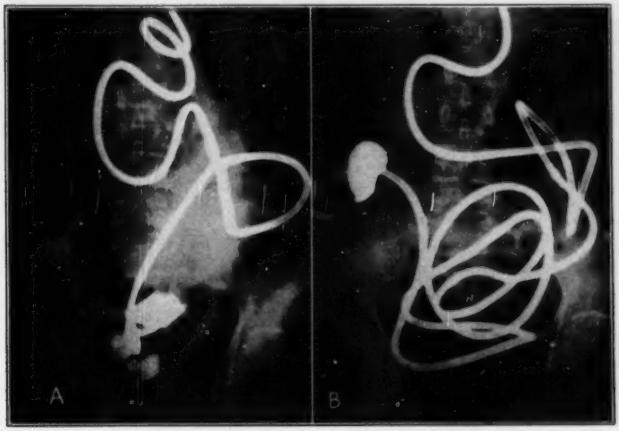

Fig. 3.—*A*, roentgenogram of patient in whom tube containing 5 cc. of mercury failed to pass in twenty-four hours. The first tube was removed, and this tube containing 9 cc. of mercury was inserted twenty-four hours before the roentgenogram was made. *B*, roentgenogram taken third day after that seen in *A*. Note the tube head in the ascending colon.

were removed and 8 to 9 cc. placed within the balloon, a successful intubation was promptly obtained. In these 15 patients intubation failed merely because sufficient mercury was not used as a propulsive agent.

A roentgenogram of a 74 year old woman with atonic ileus in whom a tube was passed which had 4 cc. of mercury within the balloon showed the tube head within the stomach at the end of twenty-four hours. Figure 3 *A* is a roentgenogram of the same patient after the first tube was removed and a second tube containing 9 cc. of mercury was passed. This roentgenogram was taken twenty-four hours after the second intubation with the increased amount of mercury. Figure 3 *B* is a

roentgenogram of the same patient taken three days after the one in figure 3 *A*. Note the position of the tube head in the ascending colon.

Roentgenograms of other patients in this group in whom the tube was passed with 5 cc. of mercury not infrequently showed the tube head still in the stomach at the end of twenty-four hours. When such tubes were removed and 9 cc. of mercury placed within the balloon, almost invariably a twenty-four hour roentgenogram demonstrated the head in the upper or middle part of the jejunum.

Figure 4 *A* is a roentgenogram of a patient with postoperative paralytic ileus for whom a tube with 5 cc. of mercury was used. This was a plastic tube. Note the position of the head of the tube at the end

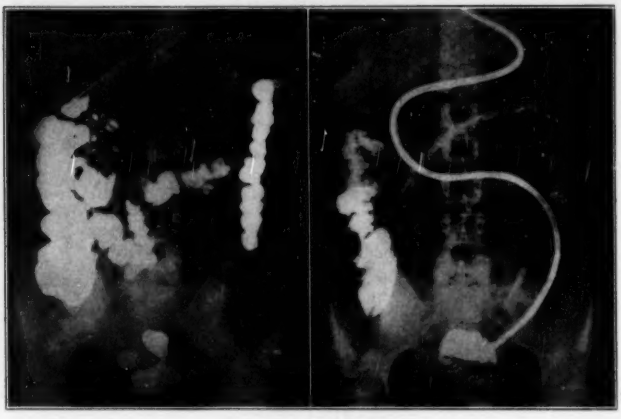

Fig. 4.—*A*, roentgenogram of a patient in whom the first tube was removed and a plastic tube with 5 cc. of mercury inserted. Note position twenty-four hours after passage of second tube. Barium in colon is residuum from diagnostic preoperative barium enema. *B*, second tube was removed and single-lumen simplified tube with 8 cc. of mercury in the balloon was then passed. This is the roentgenogram made nineteen hours after passage of the third tube.

of twenty-four hours. This tube was then removed, and a new one containing 9 cc. of mercury within the balloon was passed. This patient had undergone an ileotransverse colostomy, together with resection of the right colon, for carcinoma f the cecum. A roentgenogram taken forty-eight hours after the second tube, with the increased amount of mercury, was passed showed the tube head emerging from the anus. This result, although very dramatic, is not particularly desirable. The tubes should be removed from below in such instances, as there is no longer a need for intestinal decompression when this occurs.

A roentgenogram of a patient in whom a double-lumened tube with 5 cc. of mercury was passed showed that the tube head was still in the stomach at the end of twenty-four hours. This tube was removed, and a plastic one was passed in which the same amount of mercury was used. A second roentgenogram, taken twenty-four hours after the passage of the plastic tube, showed that the tube head was still in the stomach. The second tube was removed, and a third one was passed with 8 cc. of mercury in the balloon. Figure 4 *B* shows a roentgenogram taken nineteen hours after passage of the third tube. This patient had undergone a resection of 6 feet (182.8 cm.) of the terminal portion of the ileum as a result of thrombosis, and paralytic ileus had developed postoperatively, which rapidly responded to successful intubation. The barium in the colon was the residuum from a barium enema given preoperatively for diagnosis.

As a result of these observations, we have been able to demonstrate repeatedly that when a decompression tube containing 4 to 5 cc. of mercury is removed and the amount of mercury increased to 8 or 9 cc. in any patient in this group successful intubation is usually promptly obtained. It seems that although most patients in this group can be successfully intubated when 4 to 5 cc. of mercury is used increasing the amount of mercury to 8 or 9 cc. is necessary for some and will appreciably decrease the percentage of failures.

Group 4.—The patients in this group have an uncommon condition. They present atony of the bowel, but the illness is such that ambulation and motion cannot be carried out. Patients with fractures of the vertebrae or with malignant growths of the vertebral bodies and involvement of the cord are found in this group. Their abdomens are often distended to a degree requiring intestinal intubation. There are usually sufficient tonus and peristaltic activity to propel a lightly weighted intestinal tube downward slowly, whereas a heavily weighted one would remain in the stomach. Since the effect of motion of the patient and the effect of motion and gravity on the tube head are unobtainable in this type of patient, it is essential to use the least amount of mercury possible. We have found that the use of 2 cc. of mercury in the balloon brought about successful intubation in 2 patients of this type. Suction must be started as soon as the tube head is dropped into the stomach. By this method the stomach is emptied and a return of tonus obtained sufficient for the passage of a tube so lightly weighted. Roentgenograms taken with a bedside unit forty-eight hours after intubation showed that the tube head had left the stomach but had progressed only as far as the second portion of the duodenum. Excellent decompression was obtained in this case, although the downward progress of the tube was extremely slow.

SUMMARY

In studying 441 patients intubated over a period of three years, we have found it possible to predict with a fair degree of accuracy the amount of mercury that will result in successful intubation in most types of patients. The amount of mercury used within the balloon of tubes for intestinal decompression must be varied from 2 to 9 cc. depending on the type of patient to be intubated. Patients with paralytic ileus are generally considered as being the most difficult to intubate and also those who require intubation the most. We have found that successful and rapid intubation in such patients can invariably be obtained by increasing the amount of mercury used within the head to 8 or 9 cc. When such amounts of mercury are used, the patients must be ambulated, as we do not depend on peristaltic activity to carry the tube downward but rather on the effect of motion and the downward drag of the heavily weighted tube head seeking the most dependent level. In such cases the head will invariably be found within the midjejunum in twenty-four hours.

For patients who require intubation in whom there is no loss of peristaltic activity we have found that there is no advantage in increasing the amount of mercury used within the tube head. A tube carrying 9 cc. of mercury will not pass down the gastrointestinal tract any faster than one containing 4 cc. in any case in which peristaltic activity is the propelling force. For this reason, 4 to 5 cc. is ample and will usually result in the head of the tube being found in the jejunum at the end of twenty-four hours.

Patients who cannot be ambulated and who present an atonic distended gastrointestinal tract require a minimum of mercury in the balloon of the intestinal tube for successful intubation.

CONCLUSIONS

1. The effect of an increase in the weight within the head of tubes for intestinal decompression is far different in vivo and in vitro.

2. For the vast majority of patients in whom there is no loss of peristaltic activity 4 to 5 cc. of mercury is adequate for successful intubation.

3. Spasm of the cardiac or pyloric sphincters necessitates the use of 8 to 9 cc. of mercury in nervous, apprehensive persons.

4. Patients with atonic and paralytic ileus can be most successfully and rapidly intubated by the use of 8 to 9 cc. of mercury in the balloon of the tube. The patient is maneuvered so that the portion of the gastrointestinal tract into which the tube head is to go will be downhill and finally ambulated after the tube head has passed the duodenojejunal flexure. Motion and ambulation are absolutely essential for this group of patients when larger amounts of mercury are used as a propulsive mechanism.

666 Maccabees Building.

ACTINOMYCOSIS OF THE KNEE

Report of a Case

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C. ZENT GARBER, M.D.

AND

ALAN DeFOREST SMITH, M.D.

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ACTINOMYCOSIS has been known as a clinical disease in animals since Bollinger,[1] of Munich, first described it as lumpy jaw in cattle in 1877. Israel [2] reported the disease in human beings in 1878. Some four years later Ponfick [3] established the unity of human and bovine infections. Langenbeck,[4] Lebert,[5] Davaine,[6] Robin,[7] Revolta,[8] and Perroncito [9] had all described a syndrome resembling actinomycosis prior to Bollinger but did not definitely identify it as such. It remained for Harz [10] and for Wolff and Israel [11] to work out the bacteriology. In 1905 Wright [12] established the pathogenicity of Actinomyces bovis in this country. However, it was not until 1931 that Naeslund [13] described both anaerobic and aerobic actinomyces as being capable of causing the disease. The first clinical case in this country was reported by John B.

From the Clinic of the New York Orthopaedic Hospital.

1. Bollinger, O.: Ueber eine neue Pilzkrankheit beim Rinde, Centralbl. f. d. med. Wissenschaften **15**:481, 1877.

2. Israel, J.: Neue Beobachtungen auf dem Gebiete der Mykosen des Menschen, Arch. f. path. Anat. **74**:15, 1878.

3. Ponfick, E.: Die Actinomykose des Menschen: Eine neue Infectionskrankheit, Berlin, A. Hirschwald, 1882.

4. Langenbeck, cited by Israel,[2] p. 50.

5. Lebert, H., cited by Illich [17] and by Ruhräh.[15]

6. Davaine, cited by Ruhräh.[16]

7. Robin, cited by Illich.[17]

8. Revolta, cited by Illich [17] and by Ruhräh.[15]

9. Perroncito, cited by Illich.[17]

10. Harz: Aktinomyces bovis, ein neuer Schimmel in den Geweben des Rindes, Deutsche Ztschr. f. Thiermed. **5**:125, 1879. Footnote 1.

11. Wolff, M., and Israel, J.: Ueber Reincultur des Atkinomyces und seine Uebertragbarkeit auf Thiere, Arch. f. path. Anat. **126**:11, 1891.

12. Wright, J. H.: The Biology of the Microörganism of Actinomycosis, J. M. Research **8**:349, 1905.

13. Naeslund, C.: Experimentelle Studien ueber die Ätiologie und Pathogenese der Aktinomykose, Acta path. et microbiol. Scandinav., 1931, supp. 6, pp. 1-156.

Murphy.[14] The first complete study was done by Ruhräh,[15] who collected 1,094 cases, in none of which there was any involvement of the bones or joints. Sanford's [16] review contained 4 cases involving bone in a total of 670. Illich [17] reported the areas generally involved and found the head and neck affected in 56 per cent, the lungs in 14 per cent, the abdomen in 21 per cent and the skin in 2.6 per cent of his cases. Parker [18] in 1923 recorded 8 cases involving the vertebrae, and since that time isolated cases involving bone have been reported from time to time by other authors.[19]

REPORT OF A CASE

B. M., a white girl aged 17, was first seen at the New York Orthopaedic Dispensary and Hospital on Feb. 21, 1945, at which time she gave a history of

Fig. 1.—Enlargement of the right knee, March 10, 1945.

14. Murphy, J. B.: Actinomycosis in the Human Subject, New York M. J. **41**:17, 1885.

15. Ruhräh, J.: Actinomycosis in Man, with Special Reference to the Cases Which Have Been Observed in America, Ann. Surg. **30**:417, 605 and 722, 1899; ibid. **31**:235, 1900.

16. Sanford, A. H.: Distribution of Actinomycosis in the United States, J. A. M. A. **81**:655 (Aug. 25) 1923. Sanford, A. H., and Voelker, M.: Actinomycosis in the United States, Arch. Surg. **11**:809 (Dec.) 1925. Sanford, A. H., and Magath, T. B.: The Etiology and Laboratory Diagnosis of Actinomycosis, Minnesota Med. **5**:71, 1922.

17. Illich, A.: Beitrag zur Klinik der Aktinomykose, Vienna, J. Säfář, 1892.

18. Parker, J. B.: Actinomycosis and Blastomycosis of the Spine, J. Bone & Joint Surg. **5**:759, 1923.

injury to the right knee while swimming in July 1944. She had immediate pain, swelling and limitation of motion, all of which subsided somewhat after a few days' rest, only to recur sporadically. Activity aggravated her symptoms, and rest relieved them. On her first visit the right knee was slightly swollen (fig. 1), and there were increased heat and slight tenderness along the medial joint line. The range of motion was from 180 to 90 degrees, compared with 180 to 45 degrees on the opposite side. A roentgenogram taken at this time revealed the soft part swelling (fig. 2). One week later she was admitted for diagnostic study.

At the time of her first admission to the hospital, on March 12, 1945, the physical findings were essentially the same as on her first clinic visit. The complete blood count was normal. Mantoux and Kline tests gave negative reactions. The erythrocyte sedimentation rate was 78 mm. in one hour. On March 13 aspiration of the right knee was done, and 30 cc. of dark red fluid was obtained. Yellow

Fig. 2.—*A*, soft tissue swelling is clearly shown in this roentgenogram of the right knee, Feb. 26, 1945. *B*, the normal left knee.

flecks were present in the fluid (fig. 3). Cultures and smears revealed microaerophilic and facultatively aerobic actinomyces resembling Actinomyces bovis and "sulfur" granules surrounded by polymorphonuclear leukocytes and a lesser number of large vacuolated mononuclear cells, red blood cells and small mononuclear cells.

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19. Davies, A. B.: Actinomycosis Involving a Long Bone, Brit. M. J. **1**:705, 1932. Simpson, W. M., and McIntosh, C. A.: Actinomycosis of the Vertebrae (Actinomycotic Pott's Disease): Report of Four Cases, Arch. Surg. **14**:1166 (June) 1927. Tabb, J. L., and Tucker, J. T.: Actinomycosis of the Spine, Am. J. Roentgenol. **29**:628, 1933. Meyer, M., and Gall, M. B.: Mycosis of the Vertebral Column: A Review of the Literature, J. Bone & Joint Surg. **17**:857, 1935. Dixon, G. J.: Serological Actinomycosis with Predominant Spinal Symptoms, Including Collapse of a Vertebra, Brit. M. J. **2**:686, 1939. Lubert, M.: Actinomycosis of the Vertebrae, Am. J. Roentgenol. **51**:669, 1944.

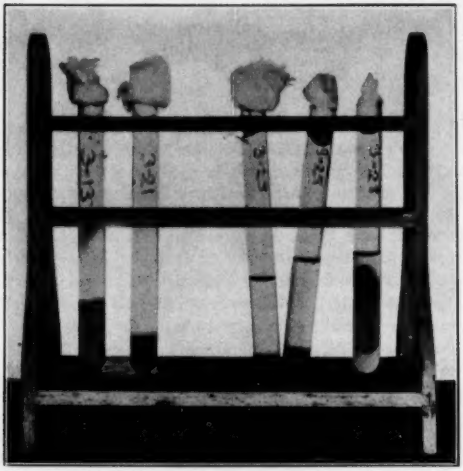

Fig. 3.—"Sulfur" granules in bloody fluid aspirated from knee joint on March 13 and March 21, 1945. There were no granules in fluid aspirated on March 25 and 28, 1945; cultures, however, give scanty growth of actinomyces.

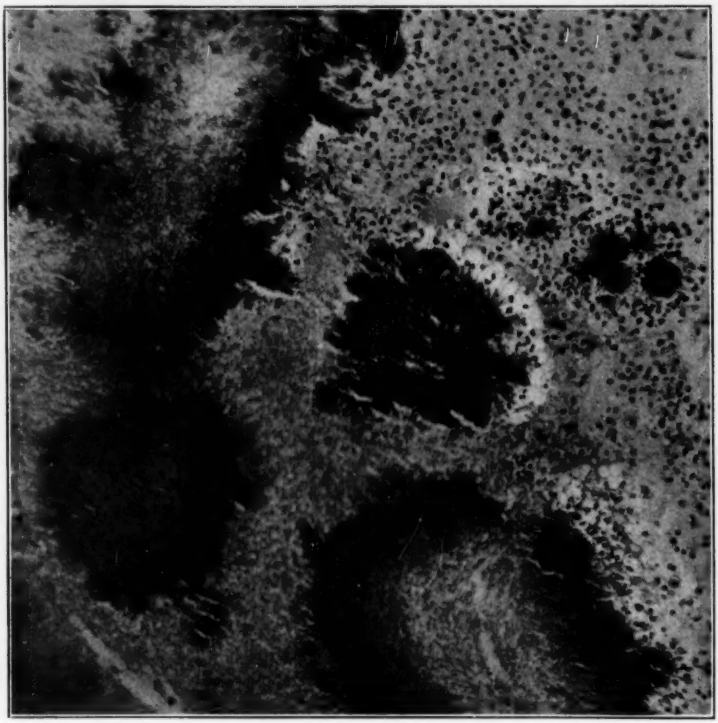

Fig. 4.—Actinomyces granules surrounded by polymorphonuclear leukocytes in fluid aspirated from knee joint on March 13, 1945. Hematoxylin and eosin stain.

The small granules appeared to be mycelia of radiating hyphae (figs. 4 and 5). Penicillin was administered intramuscularly and was injected into the knee.

The patient's temperature varied from 100 to 102 F. and her pulse rate from 100 to 120. Aspiration on May 2 revealed no fluid. The sedimentation rate fell from 78 to 38 mm. Roentgenograms of the chest and the entire spine showed a normal condition. After aspiration had been carried out four times and the patient had been treated with rest and 6,500,000 units of penicillin, she was discharged on June 9, 1945, with synovial thickening but no free fluid.

She returned to the clinic on June 15, at which time motion was full and no effusion was present. On July 20 fluid was again present, though on aspiration

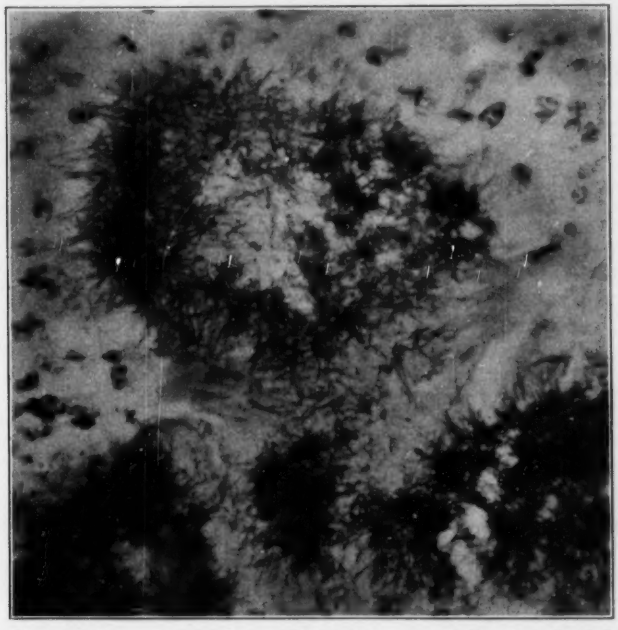

Fig. 5.—Actinomyces granule magnified to show mycelia of hyphae. MacCallum stain.

none was obtained. On July 30 still more effusion was noted. She was readmitted on September 8, and at this time in addition to joint swelling and tenderness there was an area of local tenderness 2 inches (5.08 cm.) above the superior medial border of the right patella. The range of motion was 175 to 135 degrees. A synovectomy was performed on September 24. The synovial membrane was greatly thickened with dark, partly organized granulation tissue and firmly adherent to the capsule and the medial collateral ligament. These soft granulations extended into the suprapatellar pouch, where turbid fluid was found. The disease process had broken through beneath the vastus medialis and had extended into the upper

third of the thigh. Much bleeding was encountered during the operation and postoperatively. Microscopic section revealed edematous fibrous tissue, hyperemia and infiltration of a considerable number of polymorphonuclear leukocytes, small round cells and plasma cells (fig. 6). Large phagocytic cells were particularly abundant in areas of old hemorrhage.

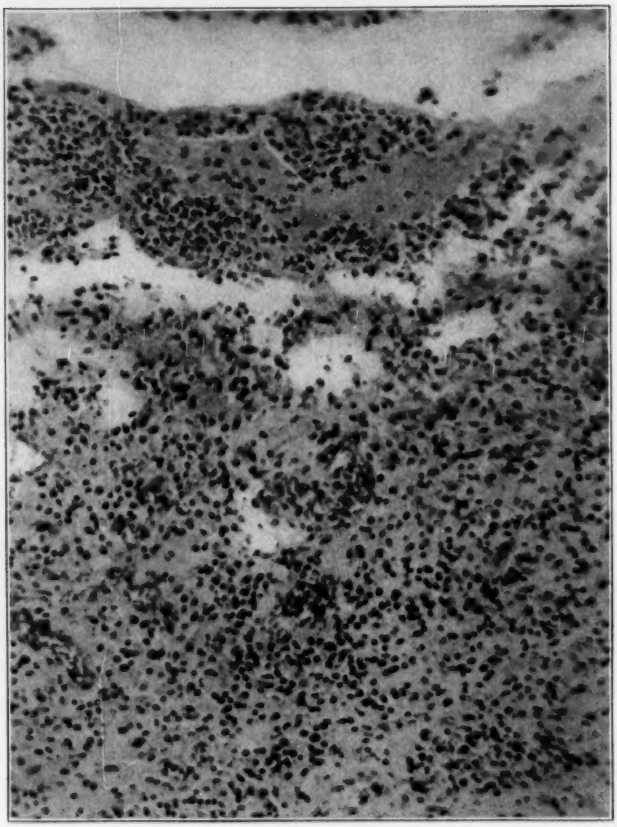

Fig. 6.—Synovial membrane of knee joint on Sept. 24, 1945, showing ulceration. There is infiltration of polymorphonuclear leukocytes, plasma cells, lymphocytes and macrophages. Hematoxylin and eosin stain.

The postoperative course was stormy, with the temperature 101 to 105 F. and the pulse rate 90 to 140. She was treated with 1,000,000 units of penicillin daily, sodium iodide, strong iodine solution and frequent transfusions.

On October 31 and November 12 abscesses of medial and lateral surfaces of the thigh were incised and drained, with local instillation of penicillin. Both times there

were found blood clots, purulent material and gelatinous masses. She gradually improved and was discharged on Jan. 7, 1946, having had 65,000,000 units of penicillin between Sept. 8 and Nov. 29, 1945. Cultures at various times showed Actinomyces bovis.

On January 16 a draining sinus was present on the medial surface of the thigh. The range of motion was 180 to 60 degrees. On January 23 the sinus had closed. On February 25 drainage was again present, and she was readmitted to the hospital on February 28 for the third time. An incision was made and drainage of the medial surface of the lower region of the thigh was done on the same day. She was discharged on March 25 with the incision healed, having had 11,000,000 units of penicillin during this stay. On her subsequent follow-up visits, the last of which was on Sept. 19, 1948, there was full motion in the right knee, mild atrophy of the quadriceps muscle and no evidence of recurrence of the disease.

Bacteriologic Findings.—The microscopic appearance of the granules in the joint fluid was typical of actinomycosis. Peripheral acidophilic clubs were seen in the fresh preparation.

Isolation cultures made on horse blood bacto® dextrose agar plates incubated aerobically, anaerobically and in an atmosphere of 10 per cent carbon dioxide; on chocolate horse blood bacto® proteose-peptone no. 3 agar plates incubated aerobically, and in an atmosphere of 10 per cent carbon dioxide, and in thioglycollate broth all showed growth of a gram-positive, non-acid-fast organism varying from rod to diphtheroid and coccoid forms and exhibiting chain formation. Soft colonies from the anaerobic plate showed a few filamentous forms. In the solid mediums the most abundant growth occurred on those incubated in an atmosphere of 10 per cent carbon dioxide, and of these the chocolate blood proteose-peptone agar alone of all the various mediums tried for isolation and subculture gave rise microscopically to some short-branched hyphae. Growth was not originally obtained in bacto® tryptose phosphate broth, but subcultures after two days of aerobic incubation produced a moderately profuse white cotton-like growth in the bottom of the tube. Growth in cooked meat medium was scanty.

Differential mediums were incubated anaerobically, with the following results: No hemolysis occurred. Gelatin was not liquefied. Litmus milk became slightly acid with precipitate formation. Acid was produced in dextrose, lactose, mannite and saccharose. There was no growth in maltose or raffinose. Aerobic fermentation reactions were the same except that no growth occurred in lactose. Salicin showed no fermentation. No growth was obtained on Löffler's medium incubated aerobically. One concluded that microaerophilic and facultatively aerobic actinomyces, resembling Actinomyces bovis,[20] was present.

COMMENT

This case is of particular interest because of the rarity of the lesion. A review of the literature has failed to reveal any case report of primary involvement of the knee joint with actinomycosis. Meyer,[21] quoted by Cope,[22] reported a somewhat similar case involving a young man who fell and injured his knee. Immobilization for six months was carried out, and finally he proved to have actinomycosis of the upper end of the

20. Bergey's Manual of Determinative Bacteriology, Baltimore, Williams & Wilkins, 1948, p. 925.

21. Meyer, M.: Infections primitives osseuses d'origine mycosique, Rev. d'orthop. **16**:624, 1929.

22. Cope, Z.: Actinomycosis, New York, Oxford University Press, 1938.

tibia. Koehler [23] in 1887 also reported a case involving the upper end of the tibia.

Etiology of Actinomycosis.—It is now generally believed that this disease is caused by an anaerobic organism present in the human mouth. Rarely, an aerobic organism found outside the body is the etiologic agent.[24] A "hayseed" or "grass chewing" history is no longer important,[25] whereas mouth and throat infections or human bites are of some significance.[26] Curiously, none of these factors was present in our case, and we were unable to demonstrate any other lesions or discover the portal of entry.

Pathologic Process.—Pathologically, actinomycosis is characterized by a chronic granuloma with extreme early vascularity, pale vacuolated cells and glistening firm connective tissue in thick strands surrounding suppurative areas, the centers of which contain the ray fungus. There is usually boardlike induration. Purplish red areas are commonly present. An earthy odor is sometimes detectable. The fluid present may be gray, white, yellow, brown or green.

Treatment.—Favorable reports have been made concerning the use of penicillin in actinomycosis both with and without surgical treatment. Herrell and Nichols,[27] at the Mayo Clinic, reported 26 cases in which penicillin was used with favorable results. In the case reported herein the use of aspiration and penicillin alone was not adequate to control the infection, and only after thorough and widespread exposure of the diseased tissues was performed in conjunction with administration of penicillin did the patient get well. At one stage it was thought that only a high amputation would save her life.

SUMMARY

A case of actinomycosis involving the knee joint has been presented. A brief historical résumé with bacteriologic and pathologic studies has been given.

The combination of widespread exposure of diseased tissues and administration of penicillin effected a cure.

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23. Koehler, A.: Aktinomykosis an der linken Tibia, Charité-Ann. **12**:599, 1887.

24. Biggert, J. H.: Actinomycosis Graminis, Bull. Johns Hopkins Hosp. **54**:165, 1934. Naeslund.[18]

25. Davis, M. I. J.: Analysis of Forty-Six Cases of Actinomycosis with Special Reference to Its Etiology, Am. J. Surg. **52**:447, 1941.

26. Cope, Z.: A Clinical Study of Actinomycosis, with Illustrative Cases, Brit. J. Surg. **3**:55, 1915. Moseley, H. F.: An Unusual Case of Actinomycosis, J. Bone & Joint Surg. **23**:359, 1941. Burrows, H. J.: Actinomycosis from Punch Injuries with a Report of a Case Affecting a Metacarpal Bone, Brit. J. Surg. **32**:506, 1945.

27. Nichols, D. R., and Herrell, W. E.: Penicillin in the Treatment of Actinomycosis, J. Lab. & Clin. Med. **33**:521, 1948.

SOLITARY CUTANEOUS AND SUBCUTANEOUS LEIOMYOMAS

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SINCE 1924, when Masson [1] described a tumor of the myoneuro-arterial glomus, clinicians and pathologists alike have been cognizant of this entity. Textbooks of pathology and surgery have made the existence of such a lesion rather common knowledge. More often than not the diagnosis of glomic tumor is made prior to microscopic study because of the characteristic severe pain, often of paroxysmal nature, and the location of the tumors in one of the extremities, commonly subungual. On the other hand, the existence of the no less common painful leiomyoma either is not appreciated or is entirely overlooked.

Stout [2] noted that as early as the eighteenth century continental writers were aware of painful tumors of the skin, generally designated tuberculum dolorosum, and that in 1873 Axel Key reported the first case of leiomyomatous tuberculum dolorosum, which involved the subcutaneous tissue of the poet Stranberg's finger. Since that time numerous reports of solitary painful leiomyomas of the skin and subcutis have appeared in the European literature. That American physicians are not so aware of this is evidenced by the fact that prior to his comprehensive report on the subject in 1937 Stout was able to find only 3 cases reported in the English language, 2 by Americans [3] and 1 by a South African.[4]

During the past ten years at the Louisville General Hospital six tumors of smooth muscle origin arising in the skin or subcutaneous tissue have been examined. Of these, four were cutaneous and two subcutaneous; of the latter, one was a leiomyosarcoma and is not included in this report.

From the Department of Pathology, University of Louisville School of Medicine.

1. Masson, P.: Le glomus neuro-myo-arteriel des regions tactiles et ses tumeurs, Lyon chir. **21**:257, 1924.

2. Stout, A. P.: Solitary Cutaneous and Subcutaneous Leiomyomas, Am. J. Cancer **29**:435, 1936.

3. Herzog, M.: A Case of Myoma of the Skin, J. Cutan. Dis. **16**:527, 1898. Ragins, A. B.: A Solitary Vascular Myoma of the Skin, Arch. Dermat. & Syph. **23**:1087 (June) 1931.

4. Wassenaar, T.: Leiomyoma of Upper Eyelid, J. M. A. South Africa **5**:818, 1931.

Four of the tumors were painful and were diagnosed clinically as neuroma, neurofibroma or glomic tumor. No history was available in 1 case. The sites were the shoulder in 2 cases, the knee in 2 and the side of the neck in 1. The duration of the lesions varied from one to twenty-five years. The age of the patients was from 21 to 62 years.

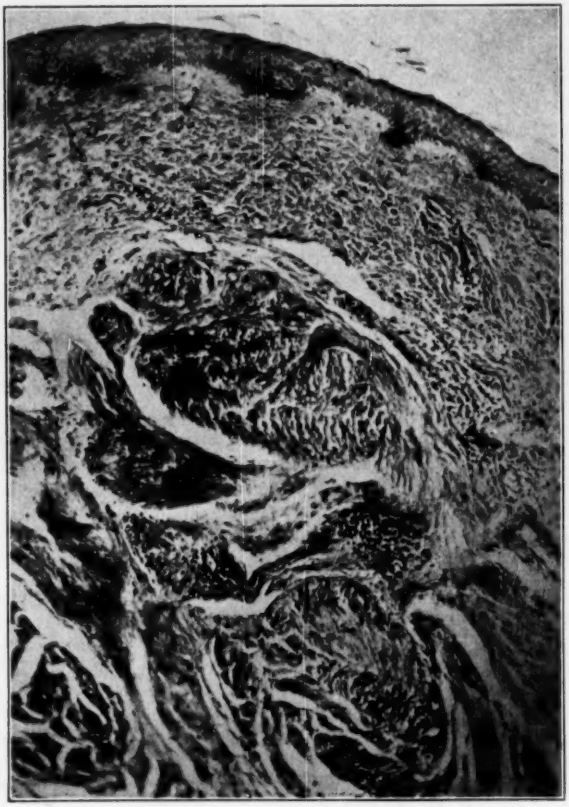

Fig. 1.—Painful leiomyoma arising from the arrectores pilorum.

The tumors varied from 3 to 10 mm. in diameter. All were well circumscribed grossly and rather firm.

Three tumors were closely associated with vessels. These vessels were thick walled, with round or often stellate lumens. The lining endothelial cells were prominent as a rule. The muscle of the vessels

often blended into and was indistinguishable from the muscle of the tumors. Other vessels were complete with adventitia. The smooth muscle was always well differentiated, with an interlacing pattern typical of leiomyomas found elsewhere. All these vascular tumors were well encapsulated.

Two tumors were well circumscribed but not encapsulated. These contained a few blood vessels which were thought to be nutritional and lacked the characteristics described for the vascular type. The well differentiated smooth muscle was again arranged in typical interlacing bundles.

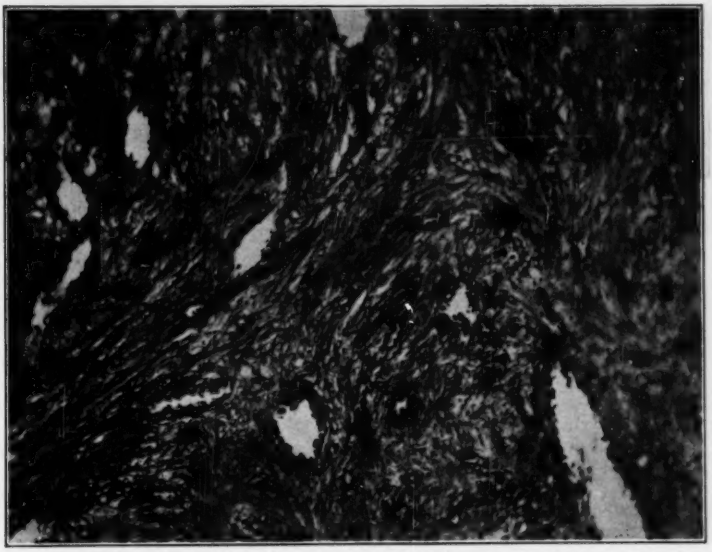

Fig. 2.—Angiomatous leiomyoma; numerous "naked" vascular channels with prominent endothelial cells.

Data on Five Cases of Solitary Leiomyoma

Case	Age	Sex	Location	Duration	Pain	Size, Mm.	Type
1	40	M	Right shoulder	25 yr.	Yes	10	Nonangiomatous cutaneous
2	30	F	Right knee	3 yr.	Yes	7	Angiomatous subcutaneous
3	21	F	Shoulder	No history	No history	6	Angiomatous cutaneous
4	40	F	Neck	No history	Yes	10	Nonangiomatous cutaneous
5	62	F	Right knee	1 yr.	Yes	3	Angiomatous cutaneous

COMMENT

That some of these tumors originate from the smooth muscle of the vessels seems apparent from histologic study; others appear to arise from the arrectores pilorum. Both Foot [5] and Stout classify them, along with glomic tumors, under tumors of peripheral nerves, although the latter was unable to demonstrate neuritis in any of the cases in which he attempted to do so. The pain associated with the lesions remains to be explained, a complicated problem because the more common multiple leiomyomas of the skin are not, as a rule, associated with pain, even though their structure is similar.

The treatment of the tumors is obviously surgical excision to provide a definite diagnosis and to relieve the annoying pain. The probability of the tumor's becoming malignant is not great; Stout found only seven leiomyosarcomas of the skin on record. Accurate clinical recognition is possible if the painful nature of solitary leiomyomas is known.

SUMMARY

Five cases of solitary leiomyoma are reported, 4 of which were cutaneous and 1 subcutaneous. The painful nature of these tumors, which is of high diagnostic value, is stressed.

5. Foot, N. C.: Histology of Tumors of the Peripheral Nerves, Arch. Path. **30**:772 (Sept.) 1940.

DELAYED SUBCUTANEOUS BERYLLIUM GRANULOMA

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AND
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IN THE past few years there has been considerable interest shown in the lesions produced by the beryllium salts. The pulmonary complications have been the most serious (involving several deaths) and have thus received the foremost attention of the investigators in this field.

The cutaneous lesions caused by beryllium poisoning, although less spectacular than the pulmonary complications, are certainly significant. Grier, Nash and Freiman [1] have outlined these lesions as follows:

1. Contact dermatitis
2. Skin ulcer
3. Lesions arising spontaneously in patients with the chronic type of lung disease (pulmonary granulomatosis)
4. Subcutaneous granuloma occurring in persons who cut themselves on fluorescent lamps

With the increase in the use of fluorescent lamps, an increase in the lesions caused by cuts from them is to be expected. Not only the industrial physician but the general practitioner and the general surgeon will see this lesion and should be familiar with its course and treatment. For this reason, the subcutaneous granuloma caused by cuts from fluorescent lamps is being emphasized.

That beryllium salts may be present in the tissues for years without producing symptoms has been established. Agate,[2] Hardy [3] and Wilson [4] have presented cases of "delayed pneumonitis" due to beryllium poison-

* From the Department of Surgery of the Youngstown Hospital Association.

1. Grier, R. S.; Nash, P., and Freiman, D. G.: Skin Lesions in Persons Exposed to Beryllium Compounds, J. Indust. Hyg. **30**:228 (July) 1948.

2. Agate, J. N.: Delayed Pneumonitis in Beryllium Worker, Lancet **2**:530 (Oct. 2) 1948.

3. Hardy, H. L.: Delayed Chemical Pneumonitis in Workers Exposed to Beryllium Compounds, Am. Rev. Tuberc. **57**:547 (June) 1948; New Clinical Syndrome: Delayed Chemical Pneumonitis Occurring in Workers Exposed to Beryllium Compounds, Bull. New England M. Center **9**:16 (Feb.) 1947.

4. Wilson, S. A.: Delayed Chemical Pneumonitis or Diffuse Granulomatosis of the Lung Due to Beryllium, Radiology **50**:770 (June) 1948.

ing arising as late as four years after exposure to beryllium compounds had ceased. Grier, Nash and Freiman [1] have shown that the lesions of the skin may also be delayed after the time of exposure.

The following case of delayed subcutaneous beryllium granuloma is being reported in an attempt to acquaint more physicians with this entity. The mere knowledge that such an entity exists is really more than half the diagnosis.

REPORT OF A CASE

A 43 year old white male pharmacist complained of a chronic ulcer on the posterior surface of the leg of four months' duration. Approximately three years

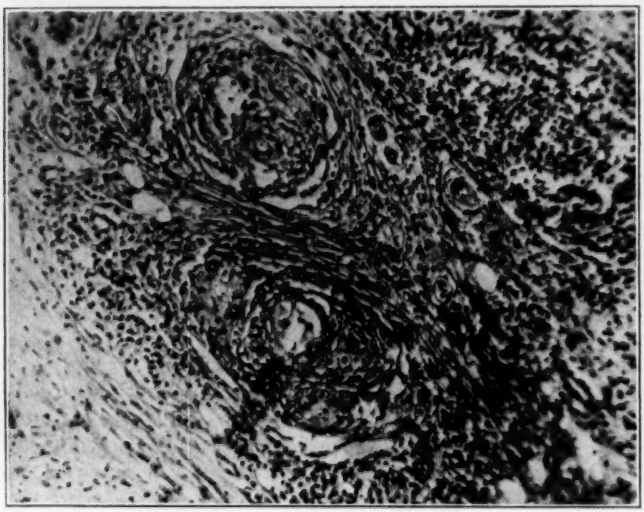

Fig. 1.—Biopsy specimen of ulcer showing tuberculoid focus.

previously he had been accidentally cut at the site of the ulcer by a broken fluorescent lamp. The wound was sutured, and primary healing had occurred. The scar was asymptomatic until four months previously. At that time he noticed that the scar had ulcerated and was "weeping," and he attributed this to frequent occasions of swimming during the summer. In spite of the application of various local antiseptics and ointments, the ulcer did not heal. It became deeper and larger, and he sought medical advice.

Physical examination disclosed an indurated, "punched-out" ulcer on the posterior surface of the leg, midway between the knee and the ankle, measuring 1 cm. in diameter. The base of the ulcer appeared to be healthy granulation tissue, with no evidence of suppuration. No varicosities or circulatory disturbances were present on either leg.

A foreign body was suspected, and under anesthesia induced by 1 per cent procaine hydrochloride the wound was probed. No foreign body was found, and so a portion of the base of the ulcer was removed for microscopic examination. The wound was left open.

Microscopic examination revealed a dense fibrous stroma in which there were tuberculoid foci with epithelioid cells, focal necrosis and many giant cells of both the Langhan and the foreign body type. No foreign body could be demonstrated in the section. The presence of tuberculosis was strongly suspected (fig. 1), but several slides prepared with Ziehl-Neelsen's stain failed to disclose any acid-fast bacilli.

The ulcer showed no signs of healing after five weeks of conservative management. A roentgenogram failed to disclose an opaque foreign body, and it was decided that the entire area should be excised.

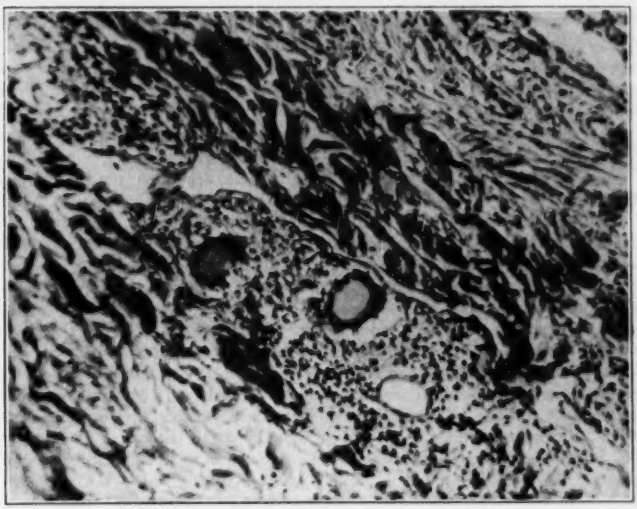

Fig. 2.—Surgical specimen of subcutaneous beryllium granuloma.

Under anesthesia induced by 1 per cent procaine hydrochloride an elliptic incision was made around the ulcer and it was deeply excised down to the fascia. A clean base was obtained, and by undermining the skin edges the wound was closed without tension. It healed by primary intention.

It was then that the lesion came to the attention of Dr. G. M. McKelvey, who suggested the possibility of its being a beryllium granuloma.

The microscopic study of the ulcer showed essentially the same picture as that described previously (fig. 2). The specimen of ulcerated skin showed considerable hyperplasia of the epithelium at the edge of the ulcer. There were disturbed polarity and local extension of the epithelial pegs, with some local invasive tendency. Occasional atypical epithelial pearls were shown near the edge of the ulcer. Under the ulcer and under the surrounding skin there were elements

of both acute and chronic inflammation, with the latter predominate. Numerous foci of epithelioid cells with slight central necrosis were shown. Many Langhan's type giant cells were shown in and around the foci. Perivascular lymphocytes and plasma cells were abundant as well as the epithelioid cells. In some places the small arteries showed distinct inflammatory reaction within their walls. There were occasional partially organized thrombi in small arterioles. Ziehl-Neelsen's stain again failed to reveal any acid-fast bacilli. The diagnosis was ulcerative chronic granulomatous and acute necrotizing inflammation (probably beryllium granuloma).

A paraffin block of tissue and a prepared slide were sent to the Edward L. Trudeau Foundation at Saranac Lake, New York, and the following report [5] was given:

Chemical Examination.—Dr. Friedrich Klemperer, head of the Department of Biochemistry, reported that 3.9 Gm. of formaldehyde-fixed tissue failed to demonstrate the presence of beryllium or at least of more than 0.05 microgram.

Examination with Ultraviolet Rays.—Microscopic examination with ultraviolet rays as a light source revealed scattered (blue) particles of magnesium tungstate, a component of fluorescent lamp powder. However, only one (bluff) particle of zinc beryllium silicate was observed.

Impression.—The pathologic picture fits the pattern of the granulomas present in a series of cases after subcutaneous implantation of fluorescent bulb powder. For the most part the lesions exhibit more collagen deposition and hyalinization than the lesions in other cases studied previously. This may have resulted from the long period between the accident and the surgical removal. The absence of beryllium on both chemical analysis and examination with ultraviolet rays does not exclude the diagnosis.

The presence of magnesium tungstate under ultraviolet rays demonstrates that at one time all components of fluorescent powder must have been present. Certainly a selective subcutaneous implantation of only one component could not have occurred. The absence of the component zinc beryllium silicate in the lesion would indicate that it disappeared from the lesion after implantation of the fluorescent powder. There are a number of cases on record in which there were similar findings. It is still to be determined whether the beryllium component disappears primarily by solution in tissue fluids, or because of fixing agents such as acid, formaldehyde or Zenker's fluid which tend to leach out the beryllium silicate.

COMMENT

A knowledge of the lesion caused by cuts from fluorescent lamps is important. Many of the cuts will not heal until the beryllium salt has been removed from the tissues, but some will heal for a time and later ulcerate. A wide excision of all cuts from fluorescent lamps is the only method to obtain a reasonable assurance of permanent cure.

5. Vorwald, A. J.: The Trudeau Foundation, Saranac Lake, N. Y., personal communication to the authors.

USE OF OXYCEL® GAUZE IN THE TREATMENT OF PERSISTENT FISTULAS

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MANY treatises have been written on involved and intricate methods for closing persistent draining fistulas, intestinal or otherwise. Most of them encompass a rather involved technic, stressing, for the most part, the utilization of nonabsorable suture material such as stainless steel or tantalum wire. Other technics utilize neighboring tissues such as muscle flaps and fascial flaps. Some procedures which have been described follow the pathway of recommending mechanical devices such as various kinds of buttons. A technic which has merit at times is the introduction of a small tube superficially into the fistula. This tube is attached to a constant suction apparatus, preferably a motor suction, and completely diverts the contents of the fistula from the surrounding skin. This in the main accomplishes the fact that the irritating fluid, whatever it may be, is kept away from the surrounding skin. Although at times the fistula may close with this treatment, often it is the feeling that persistence may be encouraged by this maneuver. However, as a temporary measure, the procedure has a place in the surgeon's armamentarium, and indeed the other procedures which have been mentioned may very well have their place in some cases.

At the outset, it is important to stress the fact that no method of closure will succeed if there is a mechanical block in the lumen of the structure with which one is dealing distal to the point of drainage. Thus, if there is an intestinal obstruction distal to the point of a persistent ileostomy opening, all methods of closure will fail. If there is an obstructing stone in the common duct distal to the origin of a persistent biliary fistula, any method of closure short of a transplantation operation (that is, dissecting out the fistulous tract and transplanting it into the intestinal tract) will be of no avail. Likewise a suprapubic bladder fistula may well persist in the presence of an obstructing prostate regardless of how many methods are utilized to close it. It must also be emphasized that a fistula originating in a structure whose secreting mechanism is well above the skin level, can rarely be closed by any procedure short of complete mobilization. By this I mean an operative procedure which involves the principle of creating new raw surface and turning in the secreting surface with layer closure.

These are time-honored and well established principles that the well trained and experienced surgeon will recognize and utilize. There is no substitute for such facts, and this paper does not propose to sidestep or deal lightly with these basic laws of surgery. I am concerned with that annoying entity which I have chosen to call the "flush fistula," that is, the condition in which the internal opening is flush with or below the skin level. It is also assumed that there is no factor of distal obstruction as proved by irrigation through and through distally and roentgenologic check-up with barium or some other opaque medium.

The method which I am here introducing is primarily based on the use of oxycel® gauze, otherwise known as oxidized cellulose gauze. The use of oxidized cellulose with thrombin as a hemostatic agent has been described by Uihlein and others.[1] A specific hemostatic action per se has been described by Frantz and Lattes.[2] They have shown that a coagulum due to the formation of salts of cellulosic acid and hemoglobin is formed. In actual surgical practice I use oxycel® always without the addition of thrombin even for hemostatic purposes. E. T. Dmytryk[3] has shown in a recently published article that oxycel® gauze implanted on traumatized peritoneal surfaces of experimental animals results in a fibroblastic proliferative process arising from the exposed connective tissue. The connective tissue cells then become flattened, which results in cells similar to normal peritoneum. There is also tubercle-like formation, with suggestive giant cell formation, owing to basophilic-staining macrophages around particles of the oxidized cellulose, which produces a picture of syncytial-like cells. Adhesions are definitely produced and are permanent. The procedure here described is purely a clinical experiment which up to date has produced results. The articles cited previously may explain in part the reason for my results, although these experiments dealt primarily with peritoneal surfaces. It is interesting, however, that the reaction was primarily a fibroblastic one. It is reasonable to assume, therefore, that within the fistulous tract per se an intense and rapid fibroblastic reaction is set up by the implantation of oxycel® gauze.

Let us assume that there is a persistent fistula intestinal in nature, for example an ileal fistula following a temporary flush ileostomy for intestinal obstruction, and suppose that a fair trial has been given to allow for primary closure. Procaine hydrochloride in a 2 per cent solution is injected intradermally around the fistula, and with a small scalpel some

1. Uihlein, A.; Clagett, O. T.; Osterberg, A. E., and Bennett, W. A.: Absorbable Oxidized Cellulose with Thrombin as a Hemostatic Agent in Surgical Procedures, Surg., Gynec. & Obst. **80**:470, 1945.

2. Frantz, V. K., and Lattes, R.: Oxidized Cellulose: Absorbable Gauze (Cellulosic Acid), J. A. M. A. **129**:798 (Nov. 17) 1945.

3. Dmytryk, E. T.: Peritoneal Reaction to Oxidized Cellulose, Arch. Surg. **56**:386 (March) 1948.

mobilization of the skin is carried out subcutaneously. The edges of the tract are also freshened with the scalpel. Oxycel® gauze is then packed snugly into the tract, a few silk sutures are introduced for skin closure and compression dressings are applied. This procedure is carried out with no discomfort to the patient. If there is no subsequent drainage discernible, the wound is inspected in four days. If there is an opening found, it is repacked with oxycel.® If there is no opening and no drainage, nothing further is done. It may be necessary to repack once or twice each time until the opening closes completely. With some fistulas, such as biliary and bladder fistulas, my colleagues and I have not bothered to suture the skin but have merely packed snugly with oxycel® and repacked when indications were present. If a small subcutaneous collection forms in the vicinity of the fistula, it should be incised.

REPORT OF CASES

CASE 1.—R. R., a 77 year old white man, was admitted to the Montefiore Hospital on Sept. 7, 1947, because of a sigmoidal lesion discovered after a barium enema. After preliminary preparation, on September 26, an obstructive resection of the involved sigmoid was performed, and the colostomy opening began to function on the seventh postoperative day. On the thirteenth postoperative day the patient began to vomit and the abdomen became distended. A flat plate of the abdomen confirmed the diagnosis of intestinal obstruction. On the fifteenth postoperative day an exploratory laparotomy was performed, and an ileostomy had to be carried out. The patient did well, and on October 21, ten days after the laparotomy, the ileostomy tube was removed. However, the ileostomy opening failed to close, and it continued to drain profusely, causing severe excoriation of the skin. It was felt that this patient could not stand another operative procedure, and, accordingly, on October 27, sixteen days after laparotomy and ileostomy, the ileostomy opening was packed with oxycel® gauze and the skin over the opening closed with several interrupted black silk sutures. Drainage from the ileostomy wound gradually became less, and the excoriated skin improved. Four days after oxycel® was packed into the tract there was practically no drainage. Seven days after there was absolutely no drainage from the ileostomy wound, and it had healed completely. The patient was discharged on November 11 with a functioning colostomy opening.

CASE 2.—E. E., a 52 year old Negro, was admitted to the Montefiore Hospital on June 6, 1948, because of intestinal obstruction secondary to a palpable rectal tumor. Two days after admission a decompression loop colostomy was performed. Anterior resection of the rectum with primary end to end anastomosis was performed on June 30, 1948. On July 7, the seventh postoperative day, the abdomen became distended, and the patient complained of severe pain in the upper abdominal area. A roentgenogram of the abdomen revealed obstruction of the small bowel. Laparotomy was performed the following day, and a kink in the small bowel was noted on the left side in the region of the previous operative site. This was straightened out, which released the obstruction. A tube ileostomy was performed proximal to the point of obstruction because of the extreme distention. The patient did well, and the ileostomy tube was removed on the eighth postoperative day. However, the ileostomy opening continued to drain profusely, even to the point of excoriating the skin. On July 21, five days after the ileostomy tube had been

removed, the wound was packed with oxycel® gauze and the skin was closed over it with several interrupted silk sutures. Three days later there was only a small amount of drainage. On July 26 the wound was repacked with oxycel® gauze. Four days later the drainage had ceased entirely. Closure of the colostomy opening was performed on Aug. 9, 1948, and the patient was discharged one month later with normal bowel function and normal sphincteric action.

CASE 3.—A. C., a 74 year old white man, was first admitted to the Montefiore Hospital on May 20, 1948, because of an incarcerated right inguinal scrotal hernia. Operation was performed by the surgical resident, and in the manipulation of the distended incarcerated bowel an opening was inadvertently made. This was immediately closed with intestinal sutures and a Bassini-Andrews herniorrhaphy performed. On the sixth postoperative day infection of the wound was evident. The drainage, which was fecal in type, continued, and a fecal fistula resulted. On June 9, 1948, three weeks after operation, he was discharged to another institution with a fecal fistula in the inguinal wound. He was readmitted six days later, on June 15, because of persistent fecal drainage from the inguinal wound. Three days after the wound was packed with oxycel® gauze and resutured loosely with interrupted skin sutures. The fistula healed. Ten days after oxycel® gauze had been inserted into the fistulous tract a small scrotal abscess developed on the right side. This was incised and drained for a few days. The patient was discharged on July 13, 1948, with both the inguinal and the scrotal wound healed and no further drainage.

CASE 4.—M. S., a 64 year old white woman, was admitted to the Montefiore Hospital because of cholelithiasis. There was a history of jaundice three years prior to her admission. Cholecystectomy was performed on Aug. 16, 1948. Exploration of the common duct was carried out at the same time, and a T tube was inserted. No stones were found in the common duct. After removal of drains in the bed of the gallbladder there was profuse drainage of biliary material around the T tube and none from the tube. The drainage was so profuse that the patient's appetite became poor, and there was extreme dehydration because of tremendous loss of fluids, electrolytes and biliary salts. It was felt that the T tube was obstructing the common duct, and so it was removed. However, the drainage continued more profusely than ever. Finally, on September 6, three weeks after operation, at which time the fistulous tract was still draining profusely, the tract was packed with oxycel® gauze and the skin closed loosely with a few skin sutures. Surprisingly enough, for the next three days the biliary drainage was much less, and on September 10 four days after the wound had been packed, it was repacked with oxycel® gauze. After this there was no drainage on the dressings. The fistula had closed, and the patient's appetite gradually increased with the cessation of biliary drainage. She was discharged on September 15, nine days after oxycel® had first been inserted, at which time the wound was healed and there was no further biliary drainage.

CASE 5.—C. S., a 75 year old white man, was admitted to the Montefiore Hospital on Sept. 14, 1948, after a barium enema had revealed the presence of a sigmoidal lesion. On September 20 a colonic resection with end to end anastomosis and a tube cecostomy flush with the peritoneum were performed. In addition, a resection of the involved dome of the urinary bladder was carried out. A Pezzer catheter was placed in the bladder and the bladder repaired about it. At the time it was noted that the patient had a tremendously enlarged prostate, and it was felt that closure of the suprapubic fistula might present a problem. Accordingly, a catheter was also introduced through the urethra. On September 22, the second

postoperative day, the patient inadvertently pulled out the cecostomy tube, and on September 27, the seventh postoperative day, the drains were completely removed. After this the dressings became soaked with urine, even though both suprapubic and urethral catheters were still in situ. On September 28 the suprapubic tube was removed, and at the same time the cavity was packed with oxycel® gauze. The wound remained dry, and the urethral catheter was removed. The patient was discharged on Oct. 10, 1948, twenty days postoperatively, with normal bowel movements and voiding normally, although somewhat frequently. The suprapubic and cecostomy wounds were completely healed.

CASE 6.—J. G., a 68 year old white man, was admitted to the Montefiore Hospital on Aug. 24, 1948, because of a rectosigmoidal lesion disclosed at the time of a barium enema and confirmed by sigmoidoscopy with biopsy. On August 30 an anterior resection of the rectosigmoid with primary anastomosis and transverse colostomy were performed. Postoperatively the patient did well, and he was discharged from the hospital on September 16 with the wound well healed and a well functioning colostomy opening. He was readmitted on October 8 for an extraperitoneal closure of the colostomy after patency of the distal anastomosis had been established by irrigations and barium enema. This was performed on October 15, and convalescence was uneventful until one week postoperatively, at which time there was evidence of a collection in the wound. This was opened, and a large amount of fecal material escaped. Fecal material continued to drain from this site, although there was some evidence of passage below the point of closure. The patient was discharged on October 31 with a persistent fecal fistula, which it was felt would close spontaneously. However, the drainage persisted, and on November 7, a week after discharge from the hospital, the fistulous tract was laid open more widely and packed with oxycel® gauze under local anesthesia. Forty-eight hours later there was little or no drainage and the cavity was repacked with oxycel.® Four days after the original packing there was little or no drainage although the fistulous tract was still present. The bowels were moving normally, and the cavity was repacked once more with oxycel® gauze. On November 18, eleven days after the original packing with oxycel,® the incision was healed. There was no further drainage from the wound.

CASE 7.—J. C., a 47 year old white man, was admitted to the Montefiore Hospital with a diagnosis of a rectosigmoidal lesion discovered at time of a barium enema. On Dec. 20, 1948, a primary resection with end to end anastomosis and a flush tube transverse colostomy were performed. One week postoperatively the bowels were moving normally and the patient was out of bed. Three days later the tube was removed from the transverse colon. Although the bowels continued to move normally, there was persistent drainage at the point of the flush tube colostomy. On Jan. 20, 1949, because of the persistent drainage, which was annoying to the patient, oxycel® gauze was packed into the narrow fistulous tract. Drainage ceased immediately, and three days later there was evidence of complete healing. However, after an enema, the tract opened up again, and there was a small pinpoint opening through which there was some passage of gas. Nothing further was done, and this closed spontaneously in forty-eight hours.

It is readily admitted that any fistula may close spontaneously and any method suggested for closure is open to suspicion for this reason. It is true also that no direct experimental procedure was performed to fortify these results. It is our feeling that experiments directed along this line may well show an intense fibroblastic proliferation in the granu-

lating tract. As a result of the irritating influence of the oxycel,® which in turn results in the obliteration of the tract, the drainage ceases. This, in addition to the mechanical effect of plugging the opening until the oxycel® begins to degenerate, would seem to result in final closure of the drainage tract. It is emphasized that there must be no factor of obstruction distal to the point of drainage and the fistula must be of the flush type, with the opening at or below the level of the skin.

I do not intend to draw the inference in this paper that none of the fistulas would have closed without the use of oxycel® gauze. Perhaps some of them would have done so spontaneously. One is dealing with animate tissues, which do have properties that at times are unpredictable. However, in the majority of cases herein presented a fair trial of spontaneous closure was conducted, without any definite results. It must be stressed that most of the patients were in the elderly age group, all of them were in poor general condition and any operative procedure carried out to close the persistent fistulas would have been a definite risk and might have even resulted in a subsequent fatality. Moreover, one could not be sure, even if one were willing to take the risk involved, that the fistula would stay closed in all instances. It appears reasonable to assert that this procedure is worth trying for persistent flush fistulas, inasmuch as it involves no operative manipulation and may be the means of clearing up a condition that is distressing to the patient and the physician alike.

SUMMARY

Seven cases of persistent urinary, biliary and intestinal fistulas have been presented in which the insertion of oxycel® gauze into the tract seemed to hasten closure.

SYNTHETIC ADHESIVES—A NEW HEMOSTATIC AGENT

A Third Report

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INVESTIGATIONS begun in September 1943 (Lowry [1]) demonstrated the practicability of controlling bleeding in abdominal viscera in animals by the application of synthetic adhesives. A large percentage of rabbits in these early experiments made uneventful recoveries after pie-shaped sections of their livers had been freshly extirpated and the ensuing gap enclosed with analogues of scotch tape.® Animals reoperated on at various intervals in which a cellophane-Buna S adhesive was used showed a considerable amount of surrounding tissue reaction, but tapes composed of a synthetic resin facing on a polyvinyl alcohol film, while not completely absorbed, were found to cause very little tissue reaction. The polyvinyl alcohol-synthetic resin combination also appeared most effective in controlling bleeding.

A more detailed study (Lowry [2]) in which polyvinyl alcohol film and synthetic resins (acrylic esters) were implanted separately within the liver, spleen, abdomen and subcutaneous tissues of a large number of rats, mice and rabbits demonstrated the superior qualities of the polyvinyl alcohol group, including an amazingly low degree of surrounding tissue reaction and a larger percentage ot apparent absorption, as evidenced by later microscopic sections of the implanted organs.

EXPERIMENTAL OBSERVATIONS

As a result of these demonstrations of the nontoxic, nonirritant effect of polyvinyl alcohol on living tissue, the possibility of polyvinyl alcohol itself evidencing hemostatic properties was investigated.

It was early recognized that studies of bleeding control and absorption on commercial polyvinyl alcohol film did not give a true criterion for

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1. Lowry, M. L.: Synthetic Adhesives in the Treatment of Wounds of the Liver and Other Surgical Conditions, Arch. Surg. **52**:160 (Feb.) 1946.

2. Lowry, M. L.: Synthetic Adhesives: Bleeding Control and Absorption Studies, Arch. Surg. **59**:147 (July) 1949.

the physiologic evaluation of this water-soluble synthetic resin. In the processing of polyvinyl alcohol into a pliable film, it is not unusual for the manufacturers to add other chemicals as plasticizers or as a means of obtaining certain desired physical attributes. It was therefore essential to prepare special polyvinyl films and solutions as well as the numerous other compounds tested in these experiments.

Evaluation of the hemostatic properties of various compounds was determined by excision, either with scalpel or scissors, of the lower one third to one half of the largest lobe of the liver of an adult rat and the local application of the test material to the freshly bleeding surface. A glass rod was the usual applicator. Except for temporary stemming of the profuse bleeding by wiping with a piece of gauze, no hemostatic material other than that being tested was brought in contact with the cut edge of the liver. Although not a completely accurate index, the more effective a hemostatic material the shorter the period of bleeding after application. In instances in which the test material effected no hemostasis, either the rat was allowed to become exsanguinated or an effective hemostatic solution was superimposed on the bleeding liver to stop the hemorrhage. All rats were anesthesized with ether. The sutures used for the abdominal incision were of linen thread. At various intervals the animals were reoperated on or they were killed and the hepatic incision sectioned and studied. Hemostatic activity was also studied by application of the material to longitudinal incisions in the spleen, which bleed less profusely than those in the liver.

Colloids other than polyvinyl alcohol were investigated by this method. When hemostatic activity was found, new compounds were formulated around the promising substance and the resulting synthesis comparatively evaluated.

Over one hundred and fifty new compounds were synthesized in this manner, various colloid adhesives being subjected to chemical and physical changes. A similar number of rats were used. Among the colloids examined were many of the gums, i. e., pectin, sodium carboxymethylcellulose and rare Japanese seaweed, gliopeltis, obtained through the kind services of Professor C. K. Tseng, of the National University of Shantung, China. None of these colloid adhesives, including polyvinyl alcohol, in aqueous solution by themselves evidenced any real hemostatic effect on the freshly bleeding edge of the liver, regardless of the concentration.

LL-81 and LL-125.—Polyvinyl alcohols vary markedly in regard to their viscosity and the degree to which they are hydrolyzed. In the

synthesis of the early solutions a medium viscosity, 91 to 93 per cent hydrolyzed polyvinyl alcohol, was used. This water-soluble resin was combined in various concentrations with pectin, sodium carboxymethylcellulose, dextrin, glucose, gum tragacanth, gum arabic, gum acacia and glycerin at different temperatures and concentrations. No obvious hemostatic action was noted in any of these solutions alone or in combination with polyvinyl alcohol.

The first solution with a demonstrable ability to check bleeding of the liver was a compound of polyvinyl alcohol and sucrose. Apparently, no other combination of sugar with polyvinyl alcohol possessed this property which, while constant, could be altered by changing the proportions of sucrose and polyvinyl alcohol. It was soon observed that a polyvinyl alcohol of low viscosity served better than a medium, and the solution most effective in stopping bleeding of the liver was LL-16. Variations in the activity of bleeding control could be obtained by making minor changes in the concentration ratio of sucrose and polyvinyl alcohol.

With LL-16 as a working standard of the ability to control bleeding, other compounds were formulated. Many interesting colloid solutions resulted which showed great variations in elastic, adhesive and tensile strength, but there was no improvement in the hemostatic effectiveness of LL-16 until LL-24 was developed, in which urea was added to the polyvinyl alcohol–sucrose mixture. Another solution, LL-37, also showed improvement in bleeding control and demonstrated the role of temperature in the colloidal synthesis.

Many other chemical groupings were attempted, with no appreciable success, until LL-81 was developed. This was a colloid synthetic compound that proved highly efficient as a nontoxic, nonirritant hemostatic agent for rat liver. A more completely hydrolyzed compound, basically related to LL-24 and LL-37, it was consistently more effective in controlling bleeding. Its superiority was demonstrated in rats, in which hemorrhage of the liver continued unabated when various other test solutions were used. The hepatic bleeding stopped completely less than two minutes after the local application of LL-81. A profuse hemorrhage, occurring after excision of three quarters of a lobe of liver, was stemmed by packing the bed of the liver with gauze saturated with LL-81 solution; the bleeding did not recur on removal of the gauze, and after abdominal closure the rat recovered.

While LL-81 proved the most satisfactory synthetic compound tested in regard to hemostatic properties, on long standing it occasionally

exhibited the phenomenon, often seen in colloids, of thixotropy, in which a solution turns into a gel. In the attempt to overcome this thixotropic phenomenon, formula LL-125 was developed, representing the addition of a measured quantity of diethanol amides of fatty acid with diethanolamine soaps in a specially treated condensation product.

Not only was LL-125 a more stable colloid solution, with little thixotropic tendency, but in comparative control tests LL-125 checked hemorrhage quicker and more effectively than LL-81, the next most satisfactory synthesis. LL-125 was therefore considered the synthetic adhesive warranting the most intensive further investigation.

STUDIES OF ABSORPTION

At various intervals after partial extirpation of the liver and spleen the rats which recovered were killed and the operative wounds studied macroscopically and microscopically; other viscera were also examined. In the case of some compounds with carboxymethylcellulose, large mucilaginous cysts were often found within the abdomen and the bladder, in many instances causing death of the animal. Such reactions were never noted with LL-16, 24, 37, 81 or 125 or with the polyvinyl alcohol compounds. In fact, the paucity of peritoneal irritation emphasizes Hueper's[3] view of the relative inertness of polyvinyl alcohol. When LL-81 and LL-125 are allowed to dry on the edge of the liver and spleen before abdominal closure, almost no intra-abdominal adhesions are to be found at subsequent reoperations.

Of the 150 rats in which the various colloidal test solutions were applied to the sectioned liver, 20 (13 per cent) died of hemorrhage within two days after the operation. Undoubtedly, a larger number would have bled to death except for the fact that at the time of operation solutions such as LL-16, 24, 37, 81 or 125 were superimposed on the cut edge of the liver to stop the hemorrhage when a particular compound was ineffective in controlling it. Two to four weeks was the usual period before reoperation and autopsy. Further sections of liver and spleen, with examination of other viscera, were performed on 35 additional rats and 10 mice in more detailed studies on absorption of colloidal solutions LL-16, 24, 37, 81 and 125. These animals were killed from two days to six months after a large slit was cut in the liver and spleen and a considerable quantity of a particular synthetic adhesive instilled in the pockets.

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3. Hueper, W. C.: Polyvinyl Alcohol Atheromatosis in Dog Arteries, Arch. Path. **31**:11 (Jan.) 1941.

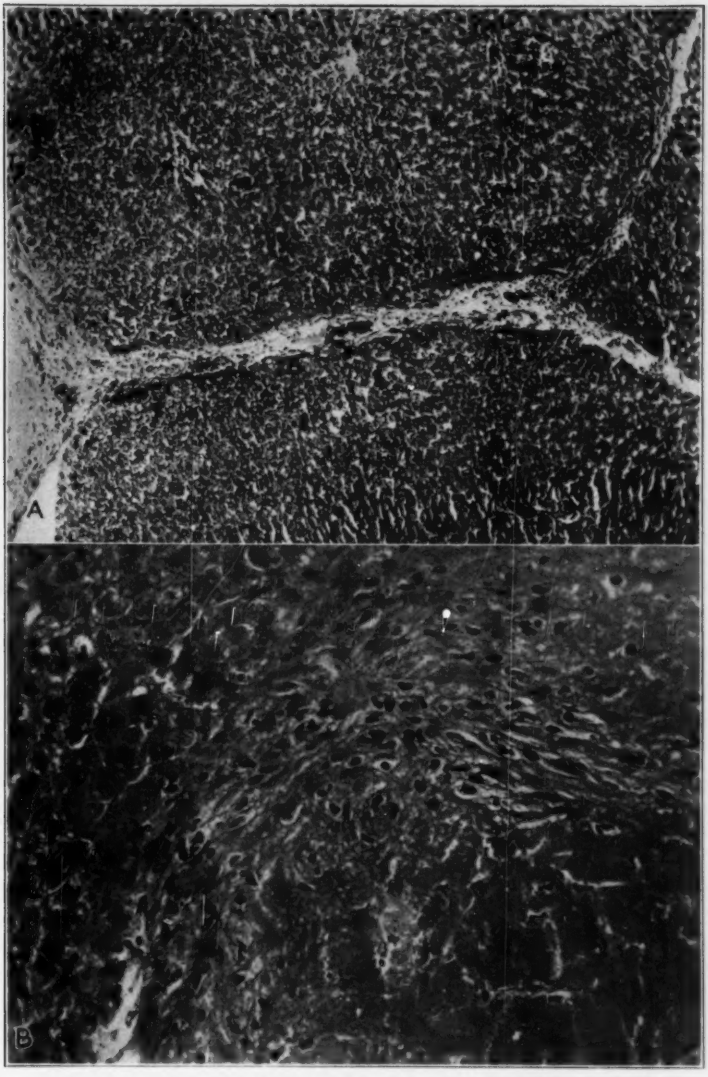

Fig. 1.—*A*, liver of rat (× 80) twenty-six weeks after pocket incision and instillation of LL-5. To the left and over the incision was stuck a specially prepared film (by the Minnesota Mining and Manufacturing Company), consisting of a polyvinyl alcohol backing with an acrylic ester adhesive facing. While the thin line of incision shows practically complete absorption of LL-5, the hepatic parenchymal cells show some vacuolization with round cell infiltration. This zone of mild hepatic damage is most apparent at the edge of the liver and may probably be attributable to the superimposed tape and particularly the acrylic esters. LL-5 is one of the earlier polyvinyl alcohols in combination with sucrose. The parenchymal cells surrounding the line of incision, except at the surface of the liver at the left, are practically normal. *B*, liver of rat (× 300) seven days after instillation of LL-125 into pocket incision. Structure and staining of hepatic parenchymal cells at right show little deviation from normal. Colloid material (LL-125) above and to left is being canalized with autolysis by young invading cells from parenchyma edge. Note absence of numerous red blood cells, also vacuolization and evidence of absorption of homogenous material at lower left.

Fig. 2.—*A*, spleen of rat (× 70) seven days after pocket excision and implantation of LL-125. Essential structure of splenic pulp practically unchanged. Lighter-staining, homogenous material in middle is implanted colloid material blending into intrinsic splenic structure, with no definite lines of demarcation or scar. A small island of round cells may be seen engulfed in the colloid material at the upper right. Note absence of hemorrhage and of inflammatory and fibrous tissue reaction, also invasion of colloid material by splenic cells. *B*, spleen of rat (× 70) twenty days after synthetic compound LL-125 has been installed into pocket incision. Although the splenic structure is fundamentally intact, the line of incision in the center can still be defined. While almost no connective scar tissue reaction is present, there are several small dark areas of absorbing hemorrhage. Note also the greatly reduced amount of homogenous-staining material (LL-125) in comparison with figure 3, in which the colloid absorption has been going on for only seven days. Vacuolization and autolysis of the synthetic adhesive has apparently advanced rapidly, so that here, twenty days after implantation, only a few small areas remain. A blending of the operative area into the splenic pulp is apparent. (All sections stained with hematoxylin and eosin; LL-125 and related colloids take on a pinkish blue tinge.)

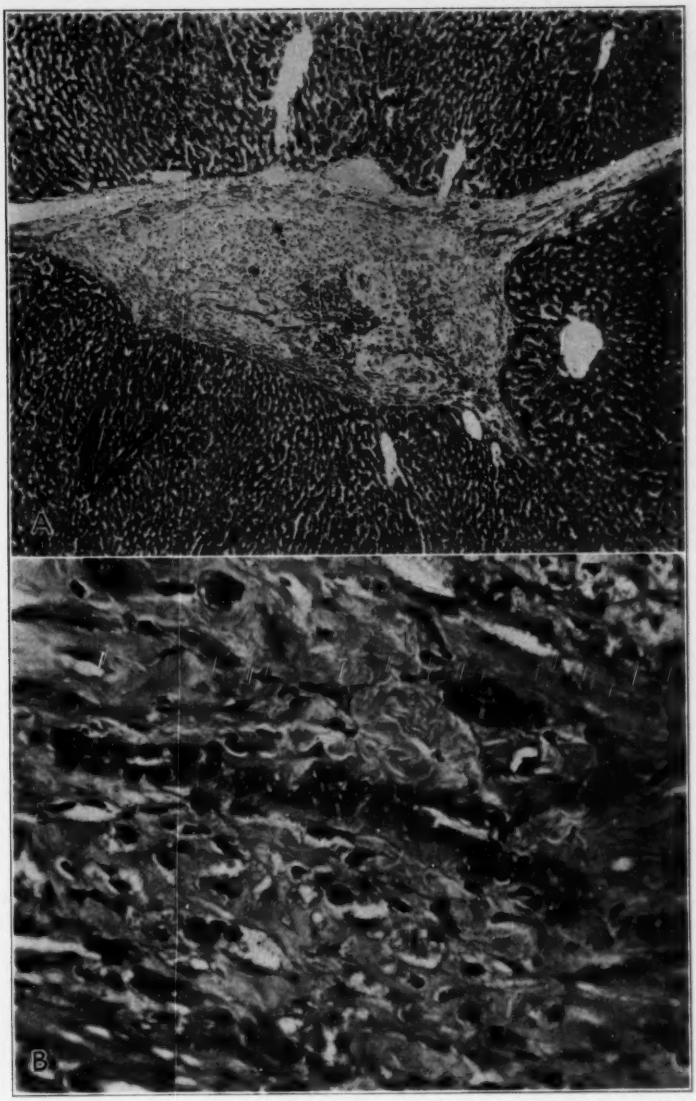

Fig. 3.—*A*, low magnification (× 42) showing colloid LL-125 deep within liver of rat. At operation, twenty days before, a wide flap pocket had been obliquely cut into the liver and a large amount of the synthetic material instilled into the hepatic aperture. Hepatic lobules and columnar structure appear normal, as does the cytoplasm of the parenchymal cells. A direct invasion of hepatic cells into the colloid material is occurring from the adjacent normal parenchyma. The typical colloid appearance is changing as the substance apparently undergoes autolysis, shrinkage and absorption. The dark specks in the middle of the colloid material are hemosiderin particles. Note particularly the absence of inflammatory or irritant scar tissue reaction. *B*, high power magnification (× 300) of portion of colloid material in middle of figure 5. The column of cells in the center represents a new bile duct invading the colloid mass; the size and cytoplasm of the cells do not appear abnormal. Invasion of other hepatic cellular elements is apparent, together with vacuolization and autolysis of synthetic colloid. Compare lesser density and absence of homogenous staining in colloid LL-125 in this section at twenty days with heavier, gelatinous appearance of colloid in figure 2, in which autolysis has proceeded for only one week. Cellular nutrition is apparently satisfactory within the colloid mass.

COMMENT

The objective of this study has been to carry to a logical conclusion the original investigation of scotch tape® synthetic adhesives begun in September 1943. No attempt has been made at this time to compare these synthetic colloid adhesives with thrombin, fibrin foam, gelfoam® (absorbable gelatin sponge) or other available hemostatic agents—a herculean project by itself.

The first investigation (Lowry [1]), demonstrated the practicability of controlling bleeding in animal viscera with synthetic adhesives. The second report (Lowry [2]), showing polyvinyl alcohol films as causing remarkably little surrounding tissue reaction, gave encouragement for the possible synthesis of a hemostatic, nonirritant polyvinyl alcohol compound, capable of absorption within the body.

While Chargaff, Bancroft and Stanley-Brown [4] found polyvinyl alcohol inactive as an anticoagulant, Hueper, Landsberg and Eskbridge [5] showed large and prolonged intravenous injections of polyvinyl alcohol to hinder clotting. Demole and Reinert [6] attempted to explain this anticoagulant action of polyvinyl alcohol as due not to a specific chemical radical but to a property common to many macromolecular substances. My experiments with topical application of polyvinyl alcohol in solution by itself have corroborated this nonhemostatic action. It is only when the polyvinyl alcohol molecule is altered by the addition of sucrose that hemostatic rather than anticoagulant properties become evident. Sugars other than sucrose do not impart this hemostatic activity, which can be further enhanced by the addition of urea and heat.

The mechanism of blood clotting is still a subject of much speculation. According to Wintrobe,[7] enzyme action may be a tenable explanation for the thrombin transformation of fibrinogen into fibrin. Ferguson [8] has proposed a colloidal disturbance theory to explain the action of prothrombin, a substance released from injured tissue cells and platelets, in activating prothrombin in the presence of calcium to form thrombin. The enmeshment of blood by a sort of superimposed foreign

4. Chargaff, E.; Bancroft, F. W., and Stanley-Brown, M.: Studies of Chemistry of Blood Coagulation, J. Biol. Chem. **115**:149 (Aug.) 1936.

5. Hueper, W. C.; Landsberg, J. W., and Eskbridge, L. C.: Effects of Intravenous and Intraperitoneal Introduction of Polyvinyl Alcohol Solutions upon Blood, J. Pharmacol. & Exper. Therap. **70**:201 (Oct.) 1940.

6. Demole, V., and Reinert, M.: Polyanetholsulfosaurer Natrium, ein neues synthetischer Mittel zur Hemmung der Blutgerinnung, Arch. f. exper. Path. u. Pharmacol. **158**:211, 1930.

7. Wintrobe, M. M.: Clinical Hematology, Philadelphia, Lea & Febiger, 1946.

8. Ferguson, J. H.: A New Blood Clotting Theory, Science **97**:319, 1943.

lattice, causing release of thromboplastin, is set forth by Jenkins and Janda [9] as a hypothetic interpretation of the hemostatic effect of gelfoam.[8]

Polyvinyl alcohol $(CH_2{:}CHOC)_x$ a water-soluble synthetic resin, is the long-chained polymerized form of vinyl alcohol, being chemically a ketose which occupies a position between sugar and starch and which lacks the acid-binding groups of the protein molecule. Polyvinyl alcohol itself has been used as a suture material (Puppel,[10] von Brandis,[11] König [12] and Braun [13]) and intravenously in the management of increased intracranial pressure (Stierlen.[14]).

Hueper and his associates gave as much as 63 Gm. of polyvinyl alcohol to dogs by intravenous infusion in divided doses in twenty-three days, with no notable findings at autopsy other than an accumulation of the colloid material in the reticuloendothelial cells of the spleen, liver, kidneys and lymph nodes and the formation of atheroma in the larger blood vessels. Excessive and repeated intraperitoneal or intravenous injections of polyvinyl alcohol given to dogs at great speed, while causing no untoward acute reaction, resulted in a reduction of erythrocytes and often in an impairment in clotting, similar to that observed after intravenous introduction of gum acacia solution.

Comparative photomicrographic study of the apparent progressive autolysis of LL-81 and LL-125 at one and three weeks and the much less complete dissolution of the polyvinyl alcohol taken in the previous report at twelve and fourteen weeks seems to imply that these new synthetic colloid compounds are more amenable to absorption by tissue fluids than plain polyvinyl alcohol solutions. Vacuolization and lightening of the colloid density together with greater hepatic cellular invasion in figure 3 *B* (at three weeks) in contrast to figure 1 *B* (one week) are evidence of the progressive autolysis. Sucrose, $C_{12}H_{12}OH$, is ordinary cane sugar. Urea, $CO(NH_2)_2$, occurs in the urine of all mammals. Neither sucrose nor urea, by itself, evidences any appreciable hemostatic action. If the proportions of the ingredients are

9. Jenkins, H. P., and Janda, R.: Studies on the Use of Gelatin Sponge or Foam as an Hemostatic Agent in Experimental Liver Resections and Injuries to Large Veins, Ann. Surg. **124**:952, 1946.

10. Puppel, E.: Klinische Ergebnisse mit Synthofil A, einem synthetischen Nahtmaterial, Zentralbl. f. Gynäk. **60**:625 (March 14) 1936.

11. Von Brandis, H. S.: Synthofil ein neues synthetisches Nahtmaterial, Zentralbl. f. Chir. **63**:372 (Feb. 15) 1936.

12. König, W.: Synthofil, ein synthetisches Nahtmaterial, Zentralbl. f. Chir. **63**:377 (Feb. 15) 1936.

13. Braun: Inaug. Diss., Leipzig, 1936.

14. Stierlen, G.: Ueber ein synthetisches Kolloid (Polyvinylalkohol) als Zusatz zu hypertonischen Lösungen und Blutersatzflüssigkeiten, Ztschr. f. d. ges. exper. Med. **106**:201, 1939.

slightly altered, or the polyvinyl alcohol viscosity or thermal conditions changed, as in compounds LL-60, 66, 77, 79, 80, 82 and 94 to 131, markedly different physical solutions result with extreme variation in hemostatic potential, as noted in the test on bleeding liver.

While none of these experiments on rats was accomplished with any regard for surgical asepsis, solutions LL-81 and LL-125 are capable of complete sterilization. Incorporated into the formula for these experiments was a 1:200,000 solution of alkyldimethyl-benzyl ammonium chloride as an astiseptic. The p_H of LL-81 and LL-125 is 7.0.

Numerous other compounds synthesized in this series, many with other sugars, not only were inadequate or increased hepatic bleeding but caused unfavorable reactions. Particularly was this true of the compounds with sodium carboxymethylcellulose, a water-soluble gum, which occasionally, by their gummy swelling, brought about death of the animal by obstruction of the intestine or bladder. No untoward reactions were observed after local application of LL-81 and LL-125. Allowing these solutions to dry completely on the cut edge of the liver in from three to five minutes resulted in a minute amount of solution required for topical application, although in cases of inaccessible bleeding gauze saturated in LL-81 or LL-125 stemmed the hemorrhage from the bed of the liver itself.

The films formed after drying of LL-81 and LL-125 are thin, elastic, tough and practically transparent. LL-125 is the more cohesive and pliable and spreads more evenly and smoothly. In a number of rats in which over half a lobe of liver was extirpated and LL-81 did not adequately stanch the hemorrhage, LL-125 apparently was the most effective hemostatic agent, the most capable of absorption and the least irritating, with LL-81 second best.

When LL-81 and LL-125 are applied to a wound or burn, a soft, pliable, nonirritant film is formed which adheres firmly to the skin and resembles epidermis. It bends freely on movement without cracking and remains in place for many hours or until washed off by water. Both LL-81 and LL-125 are dispersible in water and can readily be removed without damage to the freshly healing tissue beneath by gentle irrigation. Both of these solutions have already been used on a number of cuts, wounds and burns in man, with gratifying results. No irritation of any sort of the wound or skin has been observed to date, and bleeding from cuts is controlled. Further careful investigation in this field is necessary before large scale clinical evaluation in human beings is undertaken. However, there are many other interesting possible uses for LL-81 or LL-125, apart from hemostasis, in repair of nerves and blood vessels and in reconstructive and plastic surgery. Additional studies are in progress on various phases of synthetic adhesives described.

These experiments have established LL-125 as more effective as a hemostatic agent and probably more absorbable than LL-81. The compound LL-125 has another advantage—that of preventing thixotropy, a phenomenon in which colloid solutions often turn into a gel after standing for some time. While LL-81 may gel in from thirty to sixty days, depending on external conditions, LL-125 can remain in a fluid state for six months or longer. The other one hundred and fifty compounds examined have, for one reason or another, been found unsuitable, leaving LL-125 as the most satisfactory adhesive synthesized in this series from the standpoint of absorbability, hemostatic action, lack of irritation and toxicity plus the ability to form soft, pliable water-dispersible films.

CONCLUSIONS

Neither polyvinyl alcohol, sucrose nor urea solutions by themselves evidence any hemostatic activity when topically applied to the freshly cut surface of rat liver. When mixed together, depending on precise concentration percentages and definite thermal conditions, aqueous solutions can be synthesized which can control bleeding on local application. Of over one hundred and fifty compounds synthesized for this series, including various concentrations and viscosities of polyvinyl alcohol, sodium carboxymethylcellulose, sucrose, urea, gum acacia, gum arabic, Irish moss, dextrin, dextrose, pectin, sodium borate, boric acid, glycerin, sulfonated soya bean oil, glycine, gum tragacanth, locust bean gum and Japanese seaweed, gliopeltis, the two most effective solutions were LL-81 and LL-125.

Both of these solutions are nontoxic and nonirritant to surrounding tissue. When instilled into a pocket incision in the liver or spleen of the living rat, they are apparently capable, depending on the quantity of material inserted and other conditions, of being autolyzed by tissue fluids in from four to twelve weeks, with a minimum of connective tissue scar. Microscopic sections show invasion of the colloid material by normal hepatic and splenic cells.

Besides being apparently more effective as a hemostatic agent and at least as absorbable by tissue fluids, LL-125 is also superior to LL-81 in that the tendency to thixotropy (the propensity of colloid solutions to form gels) is practically eliminated. LL-125 differs from LL-81 in that it contains an additional minute quantity of a condensation product of diethanol amides of coconut fatty acids with diethanolamine soaps.

While the precise formula for LL-125 and LL-81 cannot be postulated at this time, the physical and physiologic differences in the individual ingredients in these compounds tend to indicate the formation of a complex new compound.

Other colloid compounds in this series, particularly those with sodium carboxymethylcellulose, have caused unfavorable reactions

and even death in rats from gelatinous obstruction of intestine or bladder. The topical application of LL-81 and LL-125 to the cut edge of the liver results in a paucity of intra-abdominal adhesions.

When applied to wounds, cuts or burns, LL-125 forms a soft pliable covering which can be readily washed away by water with no irritation to the underlying tissue. Further studies may substantiate the interesting possibilities of its use as an adhesive film in the treatment of burns, repair of blood vessels and nerves and reconstructive surgery. A nonirritating, sterile, film-forming adhesive capable of controlling bleeding and of eventual absorption, it seems not unreasonable to presume, may soon be ready for broad surgical and dermatologic evaluation in selected patients.

SUMMARY

One hundred and fifty-five new colloid adhesive compounds were synthesized, using various combinations and solution concentrations of polyvinyl alcohol, sodium carboxymethylcellulose, pectin, gum arabic, gum acacia, Irish moss, dextrin, dextrose, sucrose, urea, sodium borate, boric acid, glycerin, gum tragacanth, sulfonated soya bean oil, locust bean gum and a Japanese seaweed, gliopeltis.

The hemostatic effectiveness of each of these solutions was checked by topical application to the freshly bleeding, partially extirpated liver of healthy adult and anesthetized white rats. Many of these solutions evidenced no hemostatic qualities. The first solution with a notable ability to control bleeding was a compound of polyvinyl alcohol and sucrose. The addition of urea further improved the hemostatic action, which could be altered by slight variations in concentration of ingredients and thermal conditions. LL-81 proved the most efficient compound until the development of LL-125, to which was added a condensation product of a mixture of diethanol amides of coconut fatty acids with diethanolamine soaps. No rats died of hemorrhage after the topical application of LL-125 to the bleeding liver or spleen.

Special absorption studies were accomplished on 35 additional rats and 10 mice, in which promising compounds were instilled in pocket incisions in the liver and spleen and microscopic sections studied at different postoperative intervals. Both LL-81 and LL-125 are nonirritant to cellular tissue, and interval sections show these colloids to be progressively autolyzed in the liver and spleen, with a minimum of adhesions and scar tissue reaction. It is probable that the greatest amount of the colloid LL-125 will be absorbed by the rat liver and spleen in from four to eight weeks.

Neither polyvinyl alcohol, sucrose nor urea solutions individually exhibit hemostatic activity. Because of the changed physical and physiologic qualities, it seems probable that LL-81 and LL-125 represent completely new molecular compounds.

A number of compounds tested, particularly those with carboxymethylcellulose, caused untoward reactions and even death in the rats by obstruction of the intestine or bladder. Unfavorable reactions were not observed with LL-81 or LL-125. Both solutions can be made surgically sterile.

Besides being the more efficient hemostatic agent, and possibly more readily absorbable, LL-125 does not exhibit the thixotropic tendency found in LL-81.

When applied to wounds, cuts or burns, LL-81 and LL-125 form soft pliable elastic film coverings which can be readily washed away by water without damage to the underlying tissues.

Although further studies on these compounds are in progress, no comparative evaluation with available hemostatic agents has as yet been undertaken.

There are obvious and manifold possibilities in many surgical and dermatologic fields for an adhesive, nonirritant, film-forming, hemostatic solution capable of absorption by tissues. This investigation seems to indicate that LL-125 may be such a compound and is suitable for carefully selected evaluation in man.

The various polyvinyl alcohols examined in this report were supplied by E. I. Du Pont de Nemours and Company, the sodium carboxymethylcellulose by the Hercules Powder Company and other chemicals by Jacques Wolf and Company. Helpful cooperation was given by Dr. Clinton Thienes and other members of the departments of pharmocology and experimental medicine at the University of Southern California School of Medicine.

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RHABDOMYOSARCOMA OF THE THIGH

Report of a Case

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WHEN one considers the enormous amount of voluntary muscle tissue that comprises the human body, one is amazed at the relative infrequency of neoplastic disease in this tissue. A search of the medical literature reveals that only 208 cases of rhabdomyosarcoma have been reported.[1] This is exclusive of a series of 51 myocardial tumors which included both rhabdomyoma and rhabdomyosarcoma [2] and of cases of rhabdomyosarcoma of the vagina in children.

INCIDENCE AND SITE OF ORIGIN

In the 208 proved cases of rhabdomyosarcoma the following distribution was reported: testis, 17; orbit (eye), 19; bladder, 9; prostate, 18; spermatic cord, 1; uterus, 22; epididymis, 1, and skeletal muscle, 121. Stout [1h] has listed the rhabdomyosarcomas of skeletal muscles and given their locations as follows in his monograph: lower extremity, 52 cases (thigh, 33; leg, 18; foot, 1); upper extremity, 17 cases (arm, 9; forearm, 7; hand, 1); trunk, 31 cases (back, 11; chest, 8; buttock, 6;

From the departments of surgery and pathology, Veterans Administration Hospital.

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1. (*a*) Benison, R. L.: Sarcoma of Muscles, J. Internat. Coll. Surgeons **3**:460, 1940. (*b*) Bick, E. M.: Skeletal Muscle Sarcoma, Ann. Surg. **99**:949, 1934. (*c*) Chorache, H.: Traumatic Rhabdomyosarcoma of the Thigh, Am. J. Surg. **32**:530, 1936. (*d*) Frank, L. W.; Enfield, C. D., and Miller, A. J.: Rhabdomyosarcoma of the Neck, Ann. Surg. **104**:431, 1936. (*e*) Geschicter, C. F.: Tumors of Muscle, Am. J. Cancer **22**:378, 1934. (*f*) Harper, H. Y., and Feder, J. M.: Rhabdomyosarcoma: Report of Case Presenting Unusual Features with Reference to Age, Race, Site of Origin, and Manner of Growth, Surgery **6**:76, 1939. (*g*) Ligas, A.: Rhabdomioma, maligna del quadricipite femorali, Arch. ital. chir. **58**: 365, 1940. (*h*) Stout, A. P.: Rhabdomyosarcoma of the Skeletal Muscles, Ann. Surg. **123**:447. 1946.

2. Labate, J. S.: Congenital Rhabdomyoma of the Heart, Am. J. Path. **15**: 137, 1939.

groin, 4; abdominal wall, 2); head and neck, 19 cases (tongue, 10; neck, 6; head, 3); diaphragm, 3 cases, and psoas muscle, 1 case. It becomes apparent that the tumor develops most frequently in the skeletal muscles of the lower extremity. The case reported is one of a tumor involving the right thigh, which is the thirty-fourth known rhabdomyosarcoma involving this region of the body.

INCIDENCE AND DURATION

There is an extreme variation in the age groups afflicted by the tumor; it is found in infancy and in old age, the greatest number of cases involving patients in the fifth decade of life. The incidence is about equal in both sexes. In cases in which the duration of the disease had been recorded the average was about twenty-five months. There was 1 case of a questionable duration of fifty years. If this one is disregarded, there are no known cases of cure of the tumor.

SYMPTOMS AND SPREAD

Muscle tumors are usually asymptomatic except for local manifestations. This is the reason that most patients do not seek medical attention early. Usually the tumor is the only presenting complaint of the patient. The mass occurs, except with rare exception, without any history of trauma. It is often painless and seldom interferes with function. It may be slow growing and small and continue in this manner for many months, or its growth may be rapid. Spread of the tumor may take place through the vascular and/or lymphatic system. The lung is the commonest site of metastasis. The tumor is locally invasive and recurs frequently.

TREATMENT

In 1854 Weber [3] first described a localized tumor of the tongue of a 21 year old man. He excised the tumor, but it soon recurred. From his description of the tumor, there is little doubt that it was a rhabdomyosarcoma. The prognosis and the method of treatment have not changed much since that time. Many methods of treatment of the tumor have been employed, namely, simple excision, radical excision (amputation or disarticulation) and irradiation therapy or combinations of these methods.

Roentgen ray therapy was used as the sole method of treatment in 12 cases reported in the literature. The results were poor. In the 12 patients so treated the tumor persisted, and 10 were known to have died. The other 2 patients were not followed. Of the 49 patients reported on by Stout, 14 were given preoperative irradiation, whereas

3. Weber, C. D.: Anatomische Untersuchung einer hypertrophische Zunge nebst Bemerkungen uber die Neubildung quergestreifter Muskelfasern, Virchows Arch. f. path. Anat. 7:115, 1854.

35 were treated postoperatively. Because of the fact that these patients had surgical treatment, one cannot accurately evaluate the effect of irradiation therapy. Cases are reported in which postoperative roentgen ray treatment was given but failed to prevent local recurrences of the tumor. In a case reported by Jönsson [4] of a 65 year old woman, who had a rhabdomyosarcoma of the back excised and was given irradiation postoperatively, a local recurrence developed. The tumor was then removed by electrocoagulation, and the patient remained tumor free for nine and two thirds years and died from a complication secondary to a fracture. There have been some patients treated at Memorial Hospital by roentgen ray therapy, but the tumor was found to be resistant. The outlook is grave no matter which method of treatment is employed. Records of only 4 patients who survived symptom free for five years are reported among the 121 cases of skeletal muscle rhabdomyosarcomas collected by Stout.[1h] Only 108 of the patients received treatment. Of the 4 patients, 1 was treated by amputation alone, 1 by excision alone and the other 2 by excision and roentgen ray therapy.

There were 2 instances of long-term survival (from nine to fifty years) in which the tumor persisted, but the diagnosis was questionable. One factor which seems to be important in the prognosis of this tumor is early recognition and treatment. We cite for example a case reported by Jönsson [4] and 1 reported in the Columbia University series by Stout.[1h] Jönsson's case was of a 28 year old woman who had a tumor of the thoracic wall below the clavicle which grew rapidly for two months and was treated by excision and preoperative and postoperative irradiation. The last follow-up examination, after six years, revealed the patient to be free of any recurrence or symptoms. Stout's case [1h] was of a 31 year old woman who had a small tumor excised from within the triceps muscle only one week after it was found. The patient was alive and well five years afterward, with no evidence of recurrence or metastasis.

REPORT OF A CASE

H. H., a white man 53 years old, was admitted to the surgical service on July 29, 1948, with the complaint of a mass in the right thigh. About one year prior to his admission he noticed a feeling of soreness and tiredness in the calves of both legs on walking great distances. About one month later a small tumor developed on the anterior surface of the right thigh. The growth was not tender, and the previous pain which he had had in both calves had disappeared. The pain was then localized in the region of the right thigh. There was no history of injury or infection of this region. He experienced a tired, aching and sore feeling in the upper portion of the right lower extremity after moderate exertion. When he awakened in the morning, he would be asymptomatic. The mass was never red or particularly tender, and there was no associated lymphadenopathy in the groin

4. Jönsson, G.: Malignant Tumors of the Skeletal Muscles, Fascia, Joint Capsules, Tendon Sheaths and Serous Bursae, Acta radiol. (supp.) **36**:1, 1938.

or elsewhere in the body. There was no loss of weight, and otherwise he remained in excellent health. The tumor grew slowly and steadily until it became the size of an average lemon. Then two months prior to his admission to the hospital, the patient stated, the lesion doubled in size, without any change in symptoms. There was no particular difference in the consistency of the growth, nor was there any associated symptom other than a tired, aching, sore feeling.

The past history was noncontributory. There was no history of carcinoma or of familial diseases.

The physical examination was entirely noncontributory except that a growth was found which was limited to the right thigh. There was a mass which measured about 6 inches (15.24 cm.) in its greatest diameter (fig. 1 *A* and *B*), on the anterior surface of the right thigh at the junction of the upper and middle

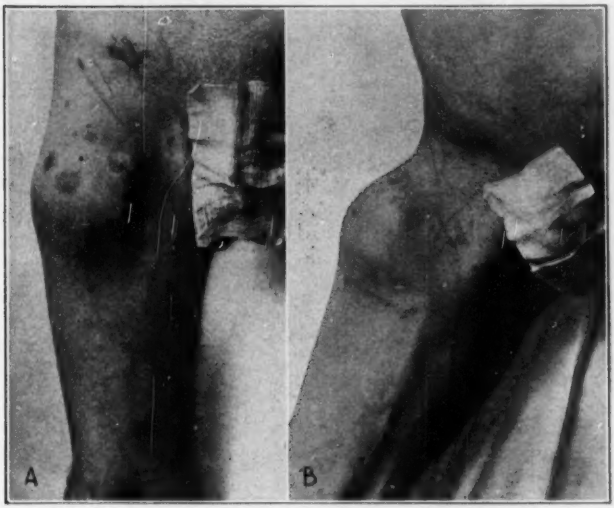

Fig. 1.—*A*, anterior view of tumor of thigh; *B*, lateral view.

thirds. It was not adherent to the skin but was mobile and seemed to be attached to the underlying quadriceps and sartorius muscles. The patient was able to tighten his quadriceps muscle and contract his knee cap. The mass felt slightly cystic on its anterosuperior medial aspect and the superior anterolateral aspect had a firm, stony-hard consistency where it appeared attached to the underlying muscle. Otherwise, there was a moderately firm consistency throughout. The muscular power of the right lower extremity was fairly good, being about equal to that of the left lower extremity. The tumor was not tender on palpation, and there was no redness or tenderness of the overlying skin. There were small shotty lymph nodes present in both inguinal areas.

The laboratory findings were essentially normal except for the white blood cell count, which was 12,700, with 81 per cent neutrophils, 17 per cent lymphocytes and 2 per cent eosinophils.

Roentgenologic examination showed no evidence of pulmonary metastasis. Studies of the upper area of the right thigh revealed a soft tissue mass over the anterior aspect of the upper third, without any evidence of bony involvement (fig. 2).

On August 4 an aspiration biopsy of the mass and the removal of an inguinal lymph node on the right side were accomplished. The pathologic report was as follows: The inguinal lymph node showed no evidence of malignancy. The biopsy of the tumor proper revealed it to be a rhabdomyosarcoma.

The case was then presented before the hospital tumor board. The recommendation made was that a radical excision of the tumor and the surrounding structures be made, followed by a course of irradiation therapy.

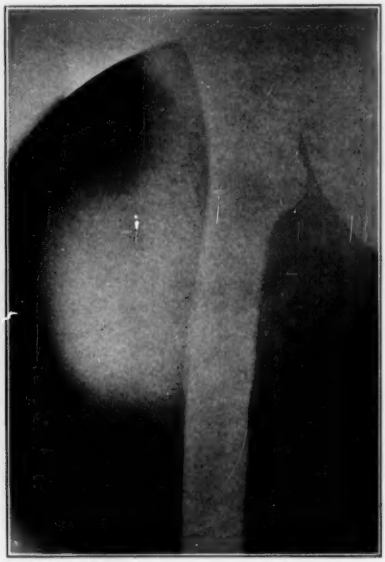

Fig. 2.—Roentgenogram of soft tissue tumor of thigh; no bony involvement.

Operation.—On August 13, under general anesthesia, a vertical, elliptic incision was made over the anterior, upper two thirds of the right thigh beginning just below the inguinal ligament, medial to the anterior-superior iliac spine and extending downward over the midportion of the thigh to about 3 inches (7.62 cm.) above the knee joint. The incision was so placed that the skin and tissue overlying the mass of the right thigh were removed.

This incision was carried through the skin, superficial fascia and fascia lata. The medial and lateral skin flaps were dissected medialward and lateralward respectively so that they would be mobilized and stay beyond the limits of the tumor. The rectus femoris muscle was then transected at its point of origin from the anterior-superior iliac spine. The tumor was movable but deeply buried in the rectus femoris muscle, from which site it most likely originated. The mass

appeared well encapsulated and roughly measured about 5 to 6 inches (12.7 to 15.2 cm.) in diameter. The sartorius muscle was likewise divided from its origin in the ilium. The dissection was then carried downward, isolating the structures in Scarpa's triangle. The femoral vessels and the great saphenous vein were preserved. The tumor showed no evidence of invading these or other structures. The fat and lymphatic vessels were excised en masse along with the tumor. The femoral nerve was dissected free as it coursed on the surface of the iliopsoas muscle. All its motor components to the remaining muscles were preserved, and only the sensory and motor portions to the muscles and skin resected were excised.

Portions of the vastus intermedius and vastus lateralis muscles were excised. The dissection was carried at least 3 inches (7.62 cm.) below the inferior limits of the tumor.

Fig. 3.—Cut section of tumor.

The lateral cut leaf of the fascia lata was sutured to the remaining portions of the vastus intermedius and vastus lateralis muscles to improve the function of extension of the leg. Two rubber drains were placed over the anterior aspect of the wound from the inguinal ligament downward and were brought out of the inferior angle of the wound.

The skin flaps were approximated by suturing the subcutaneous tissue with interrupted chromic no. 0 surgical gut. The skin was closed with mattress sutures as retention stitches, and the remaining margins were approximated with no. 00 silk. An ace® bandage was applied as a compression dressing.

Pathologic Process.—Gross Appearance: The tumor was rounded and measured 5 inches (12.7 cm.) in its greatest diameter. It weighed approximately 900 Gm. The overlying skin was unchanged, and the mass was enveloped by a thin fibrous

capsule through which was seen no evidence of extension. The surrounding muscle showed no involvement by neoplasm. The tumor was firm but not hard. On cut section, it (fig. 3) consisted of grayish, translucent, fleshy tissue which was poorly divided into irregular lobules by yellowish strands of fibrous tissue. There were interspersed areas of hemorrhage and areas of necrosis which were yellowish green.

An inguinal lymph node and portions of tissue from the region of the femoral artery showed no involvement by neoplasm.

Microscopic Appearance: The neoplasm exhibited considerable pleomorphism and was extremely cellular, with only a minimal amount of supportive stroma. The cells were arranged in compact strands and masses and formed no definite

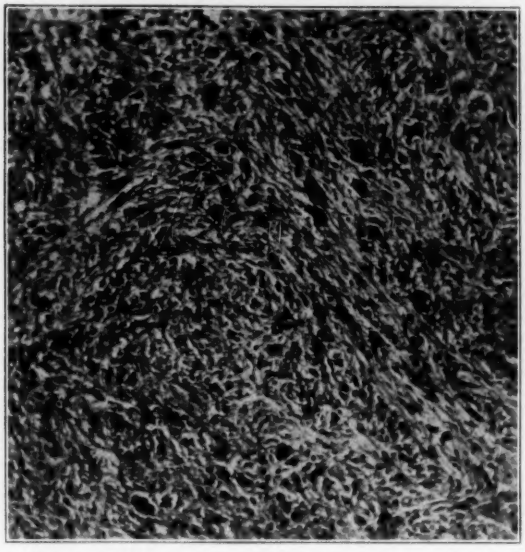

Fig. 4.—Interlacing bundles of cells showing extreme cellularity and pleomorphism. Hematoxylin and eosin stain; × 100.

structures (fig. 4). The basic cell type was a spindle-shaped cell with a round to oval vesicular nucleus and a relatively abundant, finely granular, eosinophilic cytoplasm. Occasional racquet and strap-shaped cells were present. Multinucleated giant cells were extremely numerous, and the nuclei exhibited many bizarre forms. The nuclear chromatin material was coarsely granular, and large multiple nucleoli were prominent. Mitosis was relatively frequent (fig. 5).

In some areas there were masses of large "spider-like" cells with centrally located nuclei and radiating cytoplasmic strands separated by vacuoles. The cytoplasm of these cells appeared foamy. Finely beaded longitudinal fibrils were seen in many of the cells, and an occasional spindle cell strongly suggested the presence of cross striations (fig. 6).

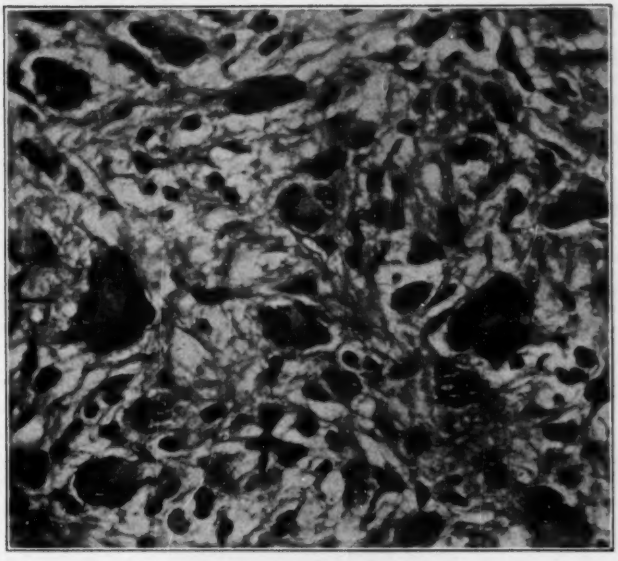

Fig. 5.—Large, bizarre, multinucleated, giant cells. Hematoxylin and eosin stain; × 500.

Fig. 6.—Spindle cells showing beaded fibrils suggesting cross striations. Hematoxylin and eosin stain; × 950.

In less cellular areas the stroma was myxomatous. Areas of necrosis and of hemorrhage were seen in many sections surrounded by reactive cellulitis and phagocytosis. Nowhere did the tumor form collagen. The neoplasm was delimited by a zone of dense fibrous tissue, and peripheral to this was a zone of active fibroplasia.

Scarlet red stains showed that the neoplastic cells contained no fat. Although definite cross striations were not seen with phosphotungstic acid stains, their demonstration is not considered necessary by many authorities. The pleomorphism

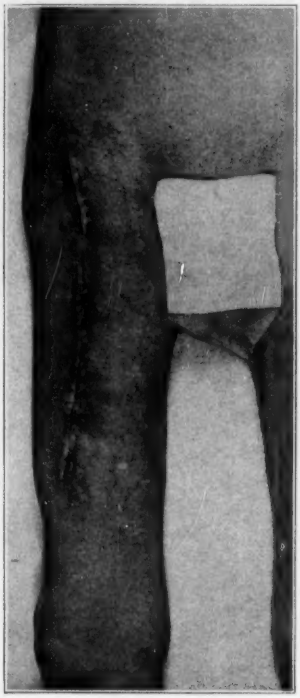

Fig. 7.—Postoperative view of thigh.

of this neoplasm, its large giant cells with huge, multiple, lobated nuclei, the abundance of glycogen within the cytoplasm, the longitudinal fibrils in many of the cells and the fact that the cells do not form collagen rather definitely establish the tumor as originating in striated muscle.

Pathologic Diagnosis.—The pathologic diagnosis was rhabdomyosarcoma.

Course in the Hospital.—The patient's postoperative course was uneventful (fig. 7). He received three courses of roentgen ray therapy. A granulating area measuring about 1 by 1 inch (2.54 by 2.54 cm.) developed in the line of the operative incision about six weeks postoperatively, which necessitated skin grafting.

It is now four months since the operation, and the patient has full use of his right lower extremity, without any evidence of limping. There is still some weakness of the quadriceps tendon, which would naturally follow removal of a large portion of the quadriceps and sartorius muscles, but because of the fact that the iliotibial band and a portion of the fascia lata were sutured to the remaining portion of the quadriceps tendon, the patient has been reeducated to use these muscles to aid in the extension of the leg.

COMMENT

In a review of the current literature on this subject, one soon realizes the difficult problem with which one is faced when it comes to deciding which is the most efficacious method of therapy for this type of tumor involving skeletal muscles. There are many articles illustrating the gross and microscopic appearance of the lesion, but there is a great deal of confusion as to the treatment of choice since the follow-up data in the series reported are incomplete and are therefore representative of only a small number of the total cases reported.

When one considers that there are only 69 cases of rhabdomyosarcoma of the extremities reported in the literature and that many of these were not followed, it becomes apparent that the best treatment to follow is dependent on the individual features present in each case. It is felt that the location, the size of the tumor, the condition of the patient and the presence or absence of local or distant metastasis are important factors in aiding the surgeon in his decision as to whether the lesion is amenable to wide local excision or amputation.

The review of the literature revealed that in a large number of cases the primary surgical excision was incomplete and inadequate, resulting in frequent local recurrences. Definite knowledge of the lesion should be obtained prior to the institution of radical treatment. Material for a biopsy removed with minimal trauma will furnish a correct diagnosis in most cases and will provide the surgeon with necessary information to carry out the proper surgical approach to the problem. In this manner a wide excision or, if necessary, amputation can be accomplished without the removal of too little or too much tissue. However, the error usually made is that the mass is not excised widely enough.

The consensus is that in cases of rhabdomyosarcoma of the extremity the treatment certainly should be radical, with the removal of a large area of normal surrounding tissues. In some instances an amputation may be necessary to accomplish this, whereas in others the location of the tumor and its size will permit a wide local excision.

It appears from all reports that this tumor is little affected by the ordinary dose of roentgen rays. It is impossible to state at this time whether or not large doses of irradiation pushed to the limit of tolerance would produce lethal action on the tumor cells.

Since the tumor in the case being reported was well circumscribed, movable, in an easily accessible area, without evidence of local or distant

metastasis and with no local bony involvement, it was felt that a wide excision of the lesion could be accomplished without producing a great deal of functional disability of the lower extremity and would offer the patient a favorable prognosis. The patient was given high voltage roentgen therapy postoperatively, too, since it was felt that no harm could be accomplished and that any cells in the regional lymphatic or blood vessels which might be present might be sensitive to the rays and be destroyed.

Early diagnosis, the institution of early adequate surgical treatment, a careful follow-up and the reporting of tumors of this type will provide the medical profession with a more complete and accurate method of treating patients with this tumor.

SUMMARY

1. A case of rhabdomyosarcoma of the right thigh which was treated by wide local excision and postoperative irradiation is presented. This is the thirty-fourth tumor of this type occurring in the thigh. In a series of 208 cases of rhabdomyosarcoma reported, the extremities were the site of involvement in 69 cases.

2. Microscopically, the tumor is characterized by spindle-shaped, racquet and strap-shaped cells, which may show cross striations, longitudinal myofibrils and multinucleated giant cells. It infiltrates insidiously and may metastasize by way of the vascular or lymphatic systems, the lungs being the most common site for distant metastasis.

3. The five year survival rate was 3.3 per cent in the series reported in the literature. The treatment instituted in the reported series was local excision, amputation and roentgen ray therapy or a combination of surgical removal and irradiation.

4. The tumor is usually resistant to roentgen therapy.

5. Accurate preoperative diagnosis by biopsy prior to institution of therapy seems indicated and will provide the surgeon with the knowledge of the nature of the tumor so that the most effective therapeutic procedure can be selected. To increase the number of five year survivals, an earlier diagnosis and a more extensive removal of the primary growth, with a greater sacrifice of grossly normal tissue about the lesion, should be carried out. An accurate follow-up of all cases should be made in order to provide members of the medical profession with an accurate picture of the prognosis of this tumor and the effectiveness of the therapy instituted.

ADDENDUM

The patient reported on has been seen on three occasions since the operation. The last follow-up was on Sept. 29, 1949, at which time there was no evidence of local recurrence or distant metastasis. He had full range of motion and good muscular power and use of the right lower extremity.

SURGICAL PROCEDURES FOR PANCREATIC LESIONS

Review of Pancreatic Surgery

RALPH F. BOWERS, M.D.
MEMPHIS, TENN.

ALTHOUGH the pancreas has been subjected to surgical procedures for a long period, not much had been accomplished until the advent of sulfonamide and antibiotic therapy in the past decade. Since this safety factor has been introduced, it has been possible to consider further pancreatic conditions requiring surgical operations and to evaluate the effectiveness of the operative therapy as such.

Surgery of the pancreas is unique in one respect. The conditions are not common enough for any one surgeon to have accumulated great experience in their treatment.

Progress has been made by patching together facts and results from many places, as in all other phases of medicine, but advances are slower because even the largest clinics have not been able to accumulate data in sufficient quantity to outline policy. Also, the operative attack on pancreatic conditions is attended with more danger in the form of morbidity and mortality than most conditions and is more difficult anatomically and physiologically in its technical phase. Normal hesitancy has, therefore, impeded this advancement. In spite of these denouement, patients seek the aid of the surgeon for pancreatic illness, and continual sidestepping is of no value in the attempt to better the surgical treatment of pancreatic conditions. It therefore is more than mildly important that the field should be surveyed, the presence of the clinical condition clarified and the methods that are safer and at the same time offer the patient the best chance for permanent cure sifted out of the known surgical procedures.

A simple classification of these conditions follows:

I. Aberrant pancreatic tissue
II. Trauma
III. Infection
    A. Acute
    B. Chronic
    C. With stones

From the Surgical Service, Veterans Administration Medical Teaching Group, Kennedy Hospital.

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IV. Neoplasms
  A. Benign
    1. Cyst
    2. Cystadenoma
    3. Islet cell adenomas
  B. Malignant
    1. Head
    2. Body
    3. Tail

ABERRANT PANCREATIC TISSUE

The clinical conditions arising from aberrant pancreas depend on the site of the displaced tissue. According to Faust [1] and others, the common sites are the stomach, duodenum, jejunum and Meckel's diverticulum. Other parts of the intestinal tract, the mesentery, mesocolon, omentum and gallbladder, are more rarely involved. Annular pancreas applies to the condition in which the pancreatic tissue surrounds the duodenum and produces symptoms of duodenal obstruction. There may be asymptomatic pancreatic rests in the stomach, intestines or mesocolon which do not demand treatment. Pancreatic tissue in the stomach obstructs if located near the pylorus and bleeds also, if ulcerated, in the same area. The intestinal diverticula produce symptoms of obstruction, hemorrhage or infection. Malignant tumors occur in this displaced tissue, more particularly in that residing in the mesocolon or mesentery. Surgical treatment of these conditions actually consists in treatment of the region involved and has little to do with a direct attack on the pancreas itself. Thus gastric resection, gastroenterostomy, intestinal resection and diverticulectomy are some of the procedures employed. Malignancy demands radical removal of the tumor, which often includes partial gastrectomy, partial colectomy, splenectomy, nephrectomy, partial pancreatectomy (tail) or a combination of these to effect a cure.

TRAUMA

The pancreas is soft and movable and is seldom torn by traumatic force, unless the trauma is due to stabbing or to a missile. Usually when compressing forces injure the pancreas, the trauma to other important structures is multiple and so devastating that the patient cannot survive. Diagnostic aids are valueless. The condition is recognized at laparotomy. The extent of the injury cannot be accurately ascertained by mere palpation of the pancreas, nor can the presence of fat necrosis be relied on to indicate trauma. It is necessary to open the gastrocolic

1. Faust, D. B., and Mudgett, C. S.: Aberrant Pancreas, with Review of the Literature and Report of a Case, Ann. Int. Med. **14**:717-728 (Oct.) 1940.

omentum and visually inspect the pancreas to learn the truth. Commonly one sees hematoma formation about the pancreas. This must be carefully studied for a wound of the penetrating type. If this is found, suture of the capsule, with drainage, is the method of choice. When the pancreas is torn extensively, so that suture is impossible, the proper method is to apply absorbable gelatin sponge (gelfoam®) to the raw surface and establish drainage. The drains lead to the outside through the opening in the gastrocolic omentum. Failure to drain may mean the loss of life for the patient.

INFECTION

Acute Pancreatitis.—This is the most popularly known condition of the pancreas. It is associated with infection or with stones in the biliary tract in a high percentage of cases. According to some authors, 70 per cent of the patients with acute pancreatitis have gallstones. The condition exists at birth and in early childhood; in many instances there are also gallstones. Recent reports by Mulholland and Doubilet [2] and others contain definite information depicting the role of regurgitation of bile into the pancreatic duct under pressure. It is believed by some that bile may normally enter the pancreatic duct, but with low pressure. Cholangiograms taken at the time of operation have demonstrated abnormal communications of a pancreatic duct with the common duct proximal to the ampulla of Vater. Opie [3] was the first to suggest that a stone impacted in the ampulla of Vater was able to direct the flow of bile into the pancreatic duct and that this would induce acute pancreatitis. He was able to prove this in the experimental animal. Accordingly, one cannot escape the facts that infection of the biliary tract, with or without stones, impacted stone in the ampulla of Vater or an abnormal connection between the common and pancreatic ducts is frequently present in acute pancreatitis and that this association must be of etiologic importance.

In other cases the etiology is not known. It is known that mumps can involve the pancreas as well as the salivary glands, a fact that suggests the possibility of an organism which produces infection by ascending the duct or through the blood stream or lymphatic vessels. So little of the truth is apparent that the definite manner in which the infection enters the pancreas is presently obscure.

Clinically, there is pain in the upper abdominal area, oftentimes sudden and severe, accompanied with shock, cyanosis, nausea, vomiting and abdominal distention. The condition is mild, moderate or fulminant, depending on the severity of symptoms. It simulates perforated duo-

2. Doubilet, H., and Mulholland, J. H.: Recurrent Acute Pancreatitis: Observations on Etiology and Surgical Treatment, Ann. Surg. **128**:609-638 (Oct.) 1948.

3. Opie, E. L.: The Etiology of Acute Hemorrhagic Pancreatitis, Bull. Johns Hopkins Hosp. **12**:182-188, 1901.

denal ulcer, gallbladder colic or perforation, renal colic, intestinal obstruction or mesenteric thrombosis if the attack is fulminant. In the milder cases it simulates ulcer, disease of the gallbladder, appendicitis and partial intestinal obstruction. Intestinal obstruction has been considered in the diagnosis at this hospital more often than any of the other conditions, so often, in fact that the diagnosis of pancreatitis is now kept in mind in all cases of atypical intestinal obstruction.

The physical findings are cyanosis, abdominal distention, tenderness, rigidity, fast pulse and lowered blood pressure and subnormal temperature at onset.

Laboratory findings reveal leukocytosis, high polymorphonuclear cell count, high serum amylase content and occasionally glycosuria. Of these tests, the blood amylase is of the greatest importance; if the amylase is markedly increased in the presence of suggestive symptomatology, it is pathognomonic.

Therapy is more definite today than ever before. Pancreatic infection is one of the acute abdominal conditions that requires the surgeon to study his case and utilize conservatism. The possibility of its presence is one of the increasing number of reasons why a surgeon no longer makes a decision in the presence of a condition known to all as a "surgical abdomen," because early operation has been shown to contribute to the fatality in many of these cases. Scandinavian surgeons were probably the first to advocate this concept in the late 1920's. The mortality rate following operation ranged from 60 to 80 per cent in the fulminating cases even in the best hands. A conservative policy resulted in a lowering of this mortality rate to the variable figures of 20 to 40 per cent, not good by any means but a great improvement. The criticism of the conservative regimen justly accused the watchful waiters of the fact that the diagnosis could not be accurately established and, therefore, that these figures and observations could not be accurate. Serum amylase studies finally clarified the situation, so that with this reliable laboratory aid the diagnosis can be satisfactorily established in the majority of cases.

Since this innovation, treatment has been conservative, with amazingly satisfactory results. The therapy consists of continuous gastric drainage, administration of penicillin or streptomycin or both, which can be started as soon as the diagnosis is suggested, and paravertebral block of the thoracic sympathetic nerves, usually in the ninth through the twelfth thoracic segments. Immediately after the block, there is often cessation of the pain. Not only are the pain fibers blocked, but probably there is also a relaxation of the sphincter of Oddi, which conceivably can allow better drainage of the pancreatic fluid into the gastrointestinal tract. The antibiotics were employed before the era of paravertebral block, and improvement was noted and mortality lowered,

although not as rapidly as after the introduction of the block. All the cases at this hospital have responded favorably to this method of therapy.

One must also include the proper procedure in event that laparotomy has been done, because the condition is still obscure and even experienced surgeons may not always be able to rely on the findings to prevent early exploration. When the abdomen is opened, one notices rust-colored fluid, edema of the omentum, fat necrosis and an enlarged, hard pancreas. To the experienced eye, the diagnosis is apparent, and this is important, because the patients do not tolerate operations well, particularly lengthy ones. In this clinic the surgeon inspects the pancreas, and if there is no softened area or one presumably containing an abscess, he immediately ceases the pancreatic exploration and explores the gallbladder. If this contains stones, removal of the stone and cholecystostomy are carried out. If an abscess in the pancreas is found, it is drained through the gastrocolic omentum. If neither pancreatic abscess nor biliary stones are found, the abdomen is immediately closed. If impacted stone in the ampulla or stones in the common duct are found, drainage of the duct with removal of the stones if that can be expeditiously accomplished, is favored. If the removal of the stones will require lengthy manipulative procedures, my colleagues and I feel that it is safer simply to drain the common duct and remove the stones at a later date. After the operation, continuous gastric suction, administration of penicillin, streptomycin or both and paravertebral block should be done with expediency. Serum amylase studies and determination of blood and urine sugar levels should be made during the postoperative course, which will guide the physician in the employment of fluids intravenously and the decision as to the length of time it is necessary to employ gastric drainage and antibodies. As convalescence favorably proceeds, a low fat diet is given, which can be changed from liquid to solid as the condition warrants.

If any one axiom can be written down for the treatment of acute hemorrhagic pancreatitis, it should be similar to the following one: "If you must operate, do not perform an extensive procedure and work quickly."

Chronic Pancreatitis.—This more obscure condition allows the surgeon time for at least a complete survey. The patient undergoes recurrent attacks of acute pancreatitis, from which he recovers, only to fear the intake of certain foods, largely fatty, which seem to induce the attacks. In the obscure form it causes indigestion and recurring pain in the upper abdominal area, radiating to the center of the back and to the left subcostal and flank regions. Occasionally, there is pain in the left shoulder like that experienced in conditions that irritate the left side of the diaphragm. There may be gallstones or stone in the common duct, or the gallbladder may have been removed after a previous attack. There

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may be pancreatic stones and calcification of the pancreas. Physical examination reveals a concerned patient who fears the attacks, is often called neurotic and not infrequently adopts the drug habit to allay his apprehension and pain. The condition can be correctly diagnosed by serum amylase studies during the acute or subacute attacks. Rarely the hardened pancreas can be palpated as a transverse, slightly tender, sausage-shaped mass in the upper region of the abdomen. Variations in the duodenal curve, gallstones, pancreatic stones and calcification of the pancreas are frequently demonstrated in roentgenograms.

The surgical treatment of these patients becomes necessary on the failure of medical treatment or dietary regulation. Few of the cases are benefited by medical measures. Certainly these should be tried, but as soon as permanent nonrelief is recognized further perserverance by the physician is not only futile but dangerous, because the patient suffers severe inanition, mental apprehension, and often becomes addicted to drugs, so that by the time he appears for surgical treatment he is not the good risk that he was months or years previously.

Surgical treatment should be employed in echelons of maneuvering. When disease of the gallbladder is present, cholecystectomy alone should be performed, because a definite number of patients will remain well if biliary infection and stones are the source of the pancreatic infection. Stones in the common duct should be removed at this time and drainage of the common duct carried out. Drainage of the common duct, if done, should be continued for a period of from two to three months in order to accomplish complete arrest of any concomitant biliary regurgitation. If no stones exist in the common duct and the latter is small and not thickened or inflamed in any manner, it appears futile to drain the duct, because the evidence then suggests that the bile coursing through the common duct is not contributing to the disease in the pancreas. However, it is advised that a small catheter be inserted into the common duct via the stump of the cystic duct through which idiopyracet injection (diodrast®) is introduced and a cholangiogram obtained for study of the sphincter of Oddi, the ampulla of Vater and abnormal communications between the pancreatic and common ducts. This is done on the operating table. Preparations for the proper filming are accomplished prior to operation and are simple. If a T tube has been inserted for drainage of the common duct the roentgenologic studies can be made at any chosen time postoperatively by simply injecting the opaque medium through the external limb of the tube.

When exploration fails to reveal disease of the gallbladder, it is advisable to insert a catheter into the common duct and study by cholangiogram the status of the ampulla and the sphincter of Oddi and the relation of the pancreatic and common ducts. Positive evidence

obtained now clearly directs the course. If regurgitation can be proved or sphincter spasm is noted, then one of three methods is available for relief:

1. Resection or transection of the sympathetic fibers supplying the region. This is accomplished by dissecting the tissues surrounding the common duct and the portal veins, which interrupts these nerve fibers. Womack has advocated extensive dissection to accomplish this. The

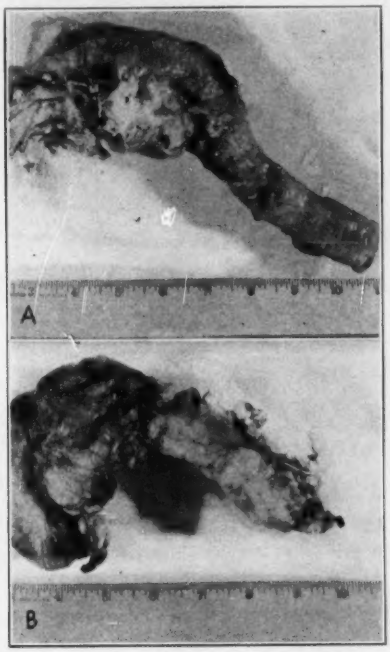

Fig. 1.—*A*, radical pancreatectomy for carcinoma of the pancreas. Favorable case. *B*, total pancreatectomy for carcinoma. The postoperative survival period was eleven months.

method interrupts pain fibers and probably induces relaxation of the sphincter and betters pancreatic and bile drainage into the duodenum. Cures have been reported but not for considerable periods. The obvious objections are, first, that it may be dangerous to shut off from the patient's cerebrum pain stimuli from this region and, second, that our experiences with sympathectomy in other parts of the body suggest that regeneration should in time occur, which will allow a return of

the factors expected to be controlled by this interruption of nerves. For these reasons, we believe that this operation should be reserved for use only if the other two types of attack fail.

2. Instrumental dilation of the sphincter of Oddi or severing of muscular fibers. Dilation of the sphincter has been practiced for years and has a few enthusiastic admirers,[4] but in the majority of hands it has

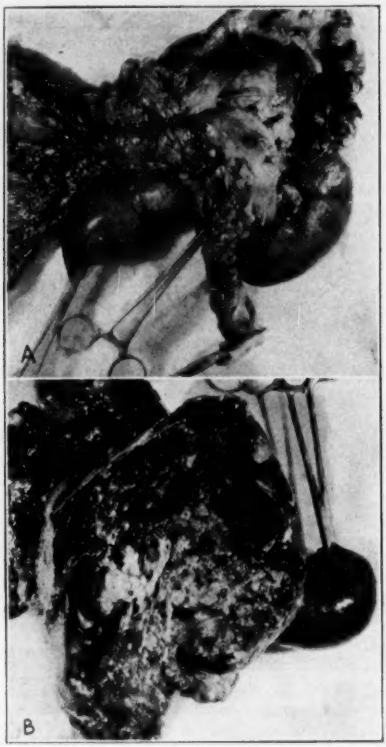

Fig. 2.—*A*, radical operation for carcinoma of the tail of the pancreas. Specimen shows partial resection of the jejunum, transverse colon and pancreas, splenectomy and nephrectomy. The postoperative survival period was five months. *B*, another view of the specimen in figure 3 showing necrosis and abscess formation in the spleen, secondary to congestion produced by carcinoma of the tail of the pancreas. No carcinoma cells were seen in the remaining splenic tissue.

4. Colp, R.; Doubilet, H., and Gerber, I. E.: Endocholedochal Section of the Sphincter of Oddi, Arch. Surg. **33**:696-707 (Oct.) 1936.

failed, because the muscles can be expected to regain their tone and spasm in time. Actually, in the cases in which there has been common duct stone or impacted ampullary stone, dilation has unintentionally accompanied the removal of the stone when the operator has passed instruments

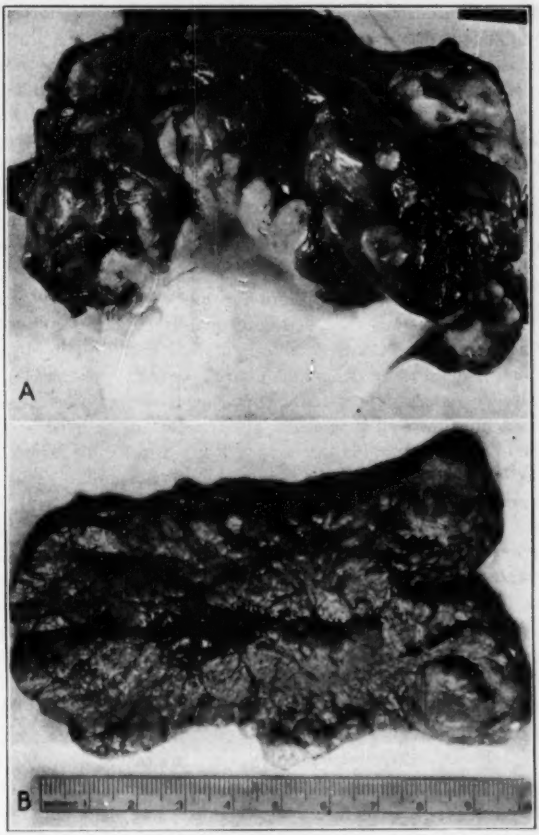

Fig. 3.—*A*, large carcinoma arising in aberrant pancreatic tissue in mesocolon. Note finger-like processes of tumor beginning to surround the transverse colon. There was no intrinsic lesion of the colon. *B*, islet cell tumor of the head of the pancreas. (Courtesy of Dr. Martin G. Goldner.)

through the ampulla to verify patency; yet the pancreatic condition persists. Also, if the regurgitation of bile is due to an entrance of the

pancreatic duct proximal to the sphincter of Oddi, dilation of the sphincter cannot be expected to effect a cure.

Doubilet and Mulholland [8] have devised an ingenious instrument called a sphincterotome which is passed through the ampulla, after which the blade of a knife is released. On withdrawal of the instrument, incision of the circular muscular ring in its anterior part is effected. Occasionally duodenotomy is required to effect this maneuver if the "blind" incision is in any way thought to be inaccurate. They have performed this operation on a small number of patients, with good results in nearly all for periods of follow-up of six months to three years. The operation in their hands has been unattended with accident, but certainly the possibility of accident exists. This is a definite contribution and should prevent regurgitation of bile into the pancreatic duct by reducing the bile pressure in the common duct even with abnormal communication. It may prove to be the operation of choice for this condition.

3. Shunting operations. These operations presuppose that the pancreatic infection is due to regurgitation of bile with pressure. Diversion of the flow of bile into the gastrointestinal tract at some distant site should accordingly effect cure. Cholangitis is a complication of this procedure and is often more dangerous than the original pancreatitis. Consequently, choledochojejunostomy, duodenostomy or gastrostomy are to be condemned as well as anastomoses between the gallbladder and the intestine or the stomach. However, the Roux-Y principle offers definite shunting with a lesser incidence of subsequent cholangitis. This operation is essentially choledochojejunostomy performed by end to end anastomosis between the proximal end of the transected common duct and the lower end of the transected jejunum. The jejunum is transected at a point about 2 feet (70 cm.) below Treitz's ligament. The lower segment is drawn through a transverse mesocolon opening and anastomosed to the open end of the common duct. It is necessary to perform jejunojejunostomy by an end to side or lateral procedure about 18 inches (45.7 cm.) below the choledochojejunal anastomosis. With this method, food and bacteria do not readily ascend the loop of quiescent jejunum and therefore cholangitis does not occur. Cole has added a kinking of the 18 inch loop by interrupted sutures which are placed in such a way as partially to obstruct the loop, which allows passage of bile but impedes the ascending progress of intestinal contents. We have employed this principle in a case involving a young man who for a period of two years had experienced recurring attacks of pancreatitis at an average rate of four attacks each month which incapacitated him so definitely that he could no longer work. He has remained entirely free from attacks since the operation of eleven months ago and has not suffered any symptoms suggestive of cholangitis. His monthly letters state that he is

absolutely well. As far as we know, he is the first patient to be treated by this method, and time alone will prove the efficacy of the procedure. Technically, the operation is not difficult, and, if proved to be permanently successful, it will offer a solution of this dreaded problem.

Chronic Pancreatitis with Stones.—Pancreatic stones and calcification of the pancreas are frequently seen in cases of chronic pancreatitis, and it is tempting to speculate that the removal of the stones or total pancreatectomy might offer the surgical cure that is so desirable. Stones are apt to be multiple, their removal is not always thoroughly possible and there is no known regimen that can be followed to assure nonrecurrence. Total pancreatectomy has been done in a few cases; in all but 1 of these a mistaken diagnosis of carcinoma had been made. This operation is accompanied with a high mortality rate and leaves the patient a cripple physiologically. Therefore, it should not be employed for benign lesions.

In regard to stones and calcification, most experienced observers do not favor the idea that surgical attack should be directed primarily at them. Numerous examples are available to demonstrate the fact that stones or calcification per se is not responsible for pancreatitis; many patients with stones or calcification are asymptomatic. Consequently, one should disregard the presence of these, pass judgment on the infection and plan to treat the pancreatitis just as if it were unaccompanied with these two findings. It would be a serious error to apply surgical treatment to the pancreas in patients who demonstrate roentgenologic evidence of stone or calcification without the symptoms of pancreatitis.

NEOPLASMS

A. Benign Neoplasms.—Pancreatic Cysts: Cysts arise in any part of the pancreas and may be present in childhood or not appear until the patient is in middle age. They are supposed to be inclusion or retention cysts, presumably from a congenital blocking of a part of the ductal system or possibly the result of unrecognized inflammation. They grow slowly and produce symptoms by pressure on the surrounding organs. Those arising in the tail or body tend to displace the stomach medially and superiorly and the transverse colon and splenic flexure downward and laterally. Those arising near the head produce symptoms of duodenal obstruction and gradually induce malnutrition. Sometimes they are associated with mild glycosuria, but this is apt to be intermittent and not alarming. The diagnosis is not too difficult if the mass is large. When it fills the upper region of the abdomen, and particularly the left upper region, it is fixed and not nodular. Roentgenologic study shows a typical displacement of the organs as described, and the displacement of the stomach and transverse mesocolon is often so definite that an accurate diagnosis can be made. The ureter can

be displaced laterally or medially, depending on the site of origin of the cyst. The kidney may be displaced superiorly or downward or not at all. Roentgenologic studies that are necessary include a series of the gastrointestinal tract, roentgenograms made after a barium enema and pyelograms. The treatment is either marsupialization, resection or internal drainage. Resection cannot be safely done in many cases because by the time the cyst has enlarged to such an extent that it produces pressure symptoms it is so large that resection often is accompanied with injury to the superior mesenteric vessels, the colic vessels or the portal vein. Therefore, only small cysts or those isolated in the tail of the pancreas, which remain small, can be handled by resection. The majority are handled by marsupialization. This is accomplished by opening and draining the cyst of its clear, viscid content, after which the edges of the opening are sutured to the abdominal wall and drains inserted. Drainage may be profuse for months and then gradually subside, with secondary healing of the wound. It is believed by some that the infection which is induced by drainage produces a sloughing of the mucosal lining, which eventually effects the cure. This does not always happen, because recurrences after marsupialization have been noted. It must be recognized that slow enlargement of the cyst is common for this condition, and it is possible that after marsupialization the period necessary for its refilling is so long that good results from this operation are noted even though total cure has not been effected. It is wise when marsupialization is done to remove a piece of the wall for histologic study because some of the apparently cystic lesions of the pancreas are actually due to neoplasm and this necessarily alters the operative procedure. Internal drainage by anastomosis of the cyst to some portion of the gastrointestinal tract has been successfully accomplished. The operation is cystojejunostomy or cystogastrostomy. It has been employed for cysts and pseudocysts with apparently great success. Chodoff [5] and Gurwitz and Hurwitz [6] have reported the performance of successful anastomosing procedures in 3 cases. Cystojejunostomy performed according to the Roux-Y principle appears to be the operation of choice if internal drainage is employed.

Cystadenoma: This condition produces symptoms similar to those of the ordinary pancreatic cyst. The difference is recognized at the time of operation. These cystic tumors tend to be multilocular and therefore do not have the smooth, concave surface like those seen in the retention cysts. They more nearly resemble nodular tumors which contain cystic areas. When the cyst wall is incised, substance in the

5. Chodoff, R. J.: Pancreatic Pseudocysts: Report of a Case Treated by Cystogastrostomy, Ann. Surg. **128**:981-986 (Nov.) 1948.

6. Gurwitz, J., and Hurwitz, A.: Treatment of Pancreatic Cysts, Ann. Surg. **128**:976-980 (Nov.) 1948.

wall and projections into the lumen of the cyst which contain tumor-like tissue can be seen. Microscopic examination shows tissue characterized by tall, columnar epithelium, which closely resembles the epithelium of the gallbladder. Papillary projections of these epithelial structures are convincing evidence of the presence of cystadenoma.

The surgical treatment of cystadenoma differs from that of cysts because, unlike a true cyst, it eventually tends to become malignant. Therefore, it is our opinion that when cystadenoma is found, resection should be done unless the operative risk is too great. We have noted that the splenic vein has coursed across the anterior surface of the mass in 4 of 5 cases[7] and that splenectomy should accompany the removal of the cystadenoma if it is located in the body or tail of the pancreas. Mild diabetes was present in 2 of the 5 cases; this promptly disappeared after operation.

Islet Cell Adenoma: This is a benign tumor which occurs in the pancreas, more commonly in the body and tail and occasionally in the head. It manifests itself by hypoglycemia and has a definite relation to the amount of food consumed in respect to the appearance of the attacks. It is seen usually in early adulthood or middle age, in both men and women. Symptoms are usually first recognized just before meals, when the patient experiences weakness, dizziness, sweating and sometimes syncope. Often the patients recognize that the lack of food is associated with his symptoms and that he can cure himself by eating. Some of them actually have carried candy or some similar edible which is taken when these symptoms appear. A typical case shows a progression and intensification of this syndrome so that the weakness and fainting spells appear within shorter periods after meals. The diagnosis is easily established by the usual blood sugar studies and glucose tolerance tests. Typically, the blood sugar will descend to an extremely low level after a period of two or three hours following the intake of food. No masses are felt on physical examination, and roentgenologic examination is not helpful. The diagnosis is, therefore, made from the history and the metabolic studies. Removal of the adenoma is the treatment of choice, and this can be extremely difficult because of the operator's inability to locate the small tumor in the substance of the pancreas. When found, it may be extremely small, globular and well circumscribed. It is usually soft and therefore can hardly be differentiated on palpation from the normal pancreatic tissue and, indeed, may have been missed in the first exploration. We have found it advisable to incise the pancreatic capsule at any suspicious sites if the tumor cannot be located after a search by an experienced surgeon. If

7. Bowers, R. F.; Lord, J. W., Jr., and McSwain, B.: Cystadenoma of Pancreas: Report of Five Cases, Arch. Surg. **45**:111-122 (July) 1942.

it cannot be located by this maneuver, resection of the outer two thirds of the pancreas is indicated. This is done because 80 per cent of the reported cases have shown that the tumors are present in the body and tail and, as is known, a small bit of nonfunctioning pancreas is all that is necessary for the maintenance of normal physiologic pancreatic life. The results of removal, either of the tumor itself or of the partial pancreatic resection which contains the tumor, are excellent. The operation should not be attended by danger. Drainage of the pancreatic stump or the site of removal is imperative.

B. Malignant Neoplasms.—From a practical viewpoint, cancer of the pancreas can be discussed under three headings: cancer of the head, cancer of the body and cancer of the tail. Pathologically, the tumors are adenocarcinomas arising from ductal or acinar epithelium and are relatively slow to metastasize. An occasional squamous cell carcinoma is seen, spoken of as a mutative phenomenon. There are only 8 reported cases of squamous carcinoma, although it is believed that there are many unreported cases or that, because of the squamous cell, the pathologist has hesitated to classify this as a pancreatic lesion. There are always present varying degrees of inflammation, the result of ductal obstruction or ulcerations of the mucosal covering. The inflammation can be disturbing at times, because the surgeon is often unable to define the exact margin of the tumor on account of the induration.

Lesions in the Head: These lesions make themselves known fairly early because they frequently arise in pancreatic tissue in the neighborhood of the ampulla of Vater and cause nonremittent obstructive jaundice, acholic stools, anorexia, nausea, fairly rapid loss of weight and an enlarged gallbladder. There is often pain at the onset, but the pain is usually milder than that seen with jaundiced conditions caused by obstructive stone in the common duct. About 56 per cent of the patients studied have experienced pain, which is diametrically the opposite of the present day textbook descriptions of an onset of "painless jaundice." Laboratory tests show acholic stools, bile in the urine and normal hepatic function if the jaundice has not been present a long time. The diagnosis is not too difficult if the gallbladder is enlarged. The liver enlarges early and becomes extremely indurated after a time. As soon as the diagnosis of obstructive jaundice is made, the patient should be prepared for early operation. This preparation demands vitamin therapy, particularly with vitamin K, chemical corrections of hypoproteinemia and the establishment of proper electrolyte and fluid balance.

During this present era, when infectious hepatitis is so common, one must include a discussion of its importance in jaundiced patients who may require surgical treatment. Hepatitis appears, with anorexia, which

soon approaches the state of abhorrence of food, jaundice, light stools, vomiting, low grade fever and an enlarged, tender liver. Laboratory tests of the blood, urine and stools aid but are not diagnostic. The gallbladder is commonly enlarged in cases of carcinoma and rarely enlarged in cases of hepatitis. The obstruction in the patient with malignant tumor is more likely to be complete, while the obstruction in the patient with hepatitis is not often complete. Itching is present in both, but the significant finding is in the liver function test; in the jaundiced patient with hepatitis there are almost always changes representative of hepatic damage indicated by the sulfobromophthalein, cephalin flocculation, thymol turbidity and prothrombin tests. Sometimes all tests demonstrate damage, and oftentimes one or two of them will give a positive reaction, but if the jaundice is due to carcinoma the liver function tests uniformly give negative reactions in the early cases. Whatever may be said of the inaccuracies of liver function tests cannot be said of their use in instances of early jaundice, because a jaundiced person with a normal reaction to liver function tests probably does not have infectious hepatitis.

Operation is best done through a transverse incision. The gallbladder is enlarged, and an inspection of the pancreas reveals a hard lump of variable size in the head, with induration and enlargement in the remaining portion. The decision of whether to advance with radical resection, which is preferably done in one stage, now has to be made.

We employ the radical operation in only the most favorable cases, that is in cases in which there is a small tumor, with mobility of the pancreas and duodenum and without extension locally or metastasis. The operation is an extensive one requiring meticulous dissection around many important structures such as the portal vein, hepatic artery and superior mesenteric vessels; the injury of any one of these may be death dealing in itself. Add to that the anastomoses for reconstruction, which are three in number and hazardous in all respects. These anastomoses include pancreaticojejunal anastomosis, choledochojejunal anastomosis and gastrojejunostomy. Consequently, the operation is attended by high mortality and morbidity rates. The operative mortality ranges from 17 to 80 per cent in the different clinics. It is now common knowledge that in the clinics in which a greater number of these cases are observed the mortality is lower than in the clinics in which an occasional case is encountered.

In our opinion the justification for the radical operation has not yet been demonstrated. It is known that a patient with carcinoma of the pancreas may live for a period of about nine months without any operation, that he may live from one year to three or four years after palliative procedures and that with the radical resection there have been only a few patients who have lived beyond a five year period. One

of the patients who survived for a long period eventually died from metastasis three years after this had been noted at a second operation. If the number of days of life for these persons is counted, it may well show that the period of survival for all patients who have carcinoma of the head of the pancreas will be greater after the palliative procedure than after the radical operation. With the high mortality rate of the radical operation, there are less patients who have a chance to enjoy longevity. This must, however, be compared with the mortality for the palliative operations, which is about 30 to 40 per cent. This figure, too, is misleading because fatalities frequently occur because the palliation is attempted in patients whose condition is poor and who are oftentimes unable to stand any operative procedure. There is much more advantage to the palliative type of operation as far as the patient is concerned than the advocates of the radical procedure admit. However, with all these facts at hand, we believe that there is enough evidence to show that the radical operation should be used in favorable cases in institutions in which the surgeons are prepared technically to perform extensive surgical procedures on the upper abdominal region and in which good methods of anesthesia, nursing care, laboratory work and replacement therapy can be carried out. We do not believe that the radical operation should be attempted in institutions in which these criteria cannot be met.

Lastly, progress will not be made in the treatment of this disease unless the radical operation is used in favorable cases and the results studied over a long period. I do not believe that it will be shown eventually that better results are obtained in favorable cases with palliative procedures than with the radical one. The palliative procedure employed for lesions in the head of the pancreas is also subject to comment. It is known that cholecystogastrostomy and cholecystoduodenostomy are not the best procedures to use because of the high incidence of cholangitis and the eventual fatty infiltration of the liver which follows them. Cholecystojejunostomy has proved to be the best, especially when it is combined with enteroenterostomy or done with the Roux-Y procedure. Either one of these two methods offers less chance of cholangitis, and good results have been obtained from their use. The operative manipulation is more extensive but not to the point where it should endanger the patient's life in the majority of the cases. If there is obstruction of the duodenum, gastroenterostomy should be employed, even if it is done at a later date, because nutrition cannot be maintained with the duodenal obstruction. For example, 1 patient obtained insurance two years after cholecystojejunostomy, although he died in the fourth year from the original carcinoma of the pancreas. Another patient, considered almost moribund, has survived one year in a supreme state of good health. These palliative operations can be done

with a mortality rate lower than 10 per cent. If they are performed in favorable cases, the mortality should approach zero per cent. I do not see that there should be any question regarding the use of the radical procedure in cases in which there is a large carcinomatous mass in the head of the pancreas which is fixed to the spine, the portal vein or the mesenteric vessels. It should not be employed in these cases because the results reveal that mortality is high and recurrence of the carcinoma or metastasis is usually prompt. The operation should not be employed to learn what can be accomplished in the way of surgical acrobatics. Total pancreatectomy has been performed for carcinoma of the pancreas and is technically easier than the partial resection of the head of the pancreas because pancreaticojejunal anastomosis does not have to be accomplished. It should be reserved for cases of carcinoma which arises either in the body or the head and extends throughout the entire pancreas yet has not metastasized or extended beyond the pancreas. The patient is a physiologic cripple and must depend on pancreatin, lipocaic and daily insulin. The control of the diabetes is not difficult if the patient eats regularly and takes the insulin regularly. Disturbances in his routine in regard to insulin therapy may prove to be quickly fatal unless accessory pancreatic tissue is present in some unsuspected part of the body. Priestley's [8] patient has survived several years without any substitutive therapy. The course in this case suggests that there is accessory pancreatic tissue in some organ or site that was unknown to the operator. Our patient who has undergone total pancreatectomy has survived nine months and has been comfortable. However, there is now metastasis to the abdominal wall and it would be surprising if he would survive a total period of one year after the operation. Total pancreatectomy should never be done for a benign lesion.

Lesions in the Body: The lesions in the body of the pancreas are amenable to surgical treatment with more ease than those located in the head, but, unlike those in the head, they are not diagnosed early and by the time laparotomy is performed they are usually large and fixed to the paravertebral structures, portal vein and mesenteric vessels. The symptoms are vague, starting usually with discomfort or distention in the upper abdominal region and pain in the back. Loss of weight is usually not rapid at first, pancreatic diarrhea is late in appearing and roentgenologic examinations do not definitely show the presence of the tumor when it is small. Better diagnostic facilities are urgently needed because if a lesion in the body could be explored when it was the size of a large marble, as is occasionally done in cases of lesions in the head

8. Priestley, J. T.; Comfort, M. W., and Radcliffe, J., Jr.: Total Pancreatectomy for Hyperinsulinism Due to an Islet Cell Adenoma: Survival and Cure at Sixteen Months After Operation; Presentation of Metabolic Studies, Ann. Surg. **119**:211-221 (Feb.) 1944.

of the pancreas, partial pancreatectomy could easily be accomplished, which would leave enough of the head of the pancreas to maintain the patient's physiologic and gastrointestinal chemistry in a normal manner and at the same time enough margin to offer him something in the way of longevity. Partial pancreatectomy requires splenectomy because one often has to sacrifice the vessels of the spleen to extirpate the outer three quarters of the pancreas completely and thoroughly.

Lesions in the Tail: Malignant tumors arising in this part of the pancreas are also difficult to diagnose when they are small. They do not impede or obstruct or invade any significant abdominal organ until they have grown to a large size or have become infected. They produce a clinical entity in the left upper quadrant for which the physician is notably hesitant to advise laparotomy. The symptomatology is often that of infection with chills, fever, loss of appetite, loss of weight and an enlarged spleen. It therefore resembles an infection similar to bacterial endocarditis, brucellosis, lymphoma, Hodgkin's disease and infarcts in the spleen due to septicemia or malaria. The enlargement of the spleen is probably the most significant physical finding. This is due to the fact that the tumor as it enlarges obstructs the splenic vein and the splenomegaly is, therefore, congestive. We have urged the use of exploratory laparotomy in any case in which the syndrome in the left upper quadrant simulates the condition just described and in which the laboratory tests do not demonstrate a definite condition of the spleen itself or the specific infections named. As a matter of fact, even if the lesion in the pancreas is not a malignant one, accurate knowledge can oftentimes be gained from the exploration. For instance, a knowledge of the presence of a lymphoma or Hodgkin's disease, the sites involved and the extension of the neoplasm is a valuable aid to the physician in directing specific therapy for these lesions.

At Kennedy Hospital we have had 1 case of squamous cell carcinoma; it arose from the tail of the pancreas and for a period of four months produced a symptom complex that resembled infection, for which the patient was given antibiotic drugs, with little response. The patient's abdomen was explored because a condition occurred which resembled perforation of a viscus, and through a left rectus incision we learned that a tumor was present in the pancreas, which had become infected and perforated into the lesser peritoneal sac and that, in turn, had perforated into the free peritoneal cavity. We correctly diagnosed the condition at laparotomy as a malignant tumor which arose in the tail of the pancreas. Drainage was instituted and the use of antibiotics continued. One month later we reexplored and resected the tumor, which required partial pancreatectomy, partial resection of the jejunum, partial resection of the transverse colon, splenectomy and left nephrectomy. The patient was left with a colostomy opening in the right

transverse colon and the site of operation was drained. He lived five and a half months after this operation, during which time he stayed at home with his family. Had it been possible to explore the abdomen when the tumor was small, the operation would have been of less radical extent and a longer period of survival certainly could have been expected. Actually, the resection of the tail of the pancreas is simple compared to the removal of the head. It means that the pancreas must be transected either at the level of the portal vein or just to the left of it. The raw surface of the pancreas is sutured with mattress sutures and the spleen removed with the tail. A drain must be placed at the stump of the pancreas which emits through the abdominal wall via the gastrocolic omentum. Surgical intervention in the tail of the pancreas is not difficult. The diagnosis of the early lesion is extremely difficult and, in my opinion, cannot be established unless early exploratory laparotomy is employed for obscure lesions in the left upper quadrant.

CARCINOMA IN ABERRANT PANCREAS

It is suspected that this is a more common lesion than is realized and as such has no symptomatology or clinical picture which is typical. It is known that aberrant pancreatic tissue, wherever it may be, is subjected to the possibility of malignant degeneration. It is also known that some of the reports of the removal of malignant tumors from the abdomen state that the tumors are of the adenocarcinoma or squamous cell type and that the pathologists suggest that they are of pancreatic origin but because the pancreas itself is uninvolved they are not classified as aberrant pancreatic tumors. Consequently, the accurate incidence of malignancy in cases of aberrant pancreatic tissue is not known.

It should be suspected that malignant tumors in the mesocolon or in the mesentery or intestinal diverticula have arisen in pancreatic rests, because the rests are seen in these positions. The most convincing evidence occurs in a case that we observed last year at Kennedy Hospital. This patient consulted us because he had noticed a mass in the left upper quadrant which had increased in size over a period of eighteen months and produced no symptoms until it became so huge that he sought advice, partly from curiosity and partly from apprehension. He had not lost weight or suffered pain and did not even suffer with indigestion. The tumor had pushed the stomach superiorly and the transverse colon inferiorly and extended from the region of the spleen across the abdomen to the right of the midline. Although it could not be distinguished from the spleen, it was felt that it arose from the tail of the pancreas. It was too hard in texture to be a pancreatic cyst or a cystadenoma of the pancreas, and therefore a malignant tumor in the tail of the pancreas was suspected. At operation we noticed a large tumor which was slightly movable and resting in the transverse meso-

colon. It was beginning to surround the transverse colon and had obstructed it moderately. After a considerable amount of dissection, it was obvious that it arose in the transverse mesocolon, could easily be freed from the pancreas, the duodenum and the kidney and did not involve any significant vessels. It was removed in its entirety with a large segment of transverse colon and the spleen. Microscopic section showed it to be squamous cell carcinoma with changes similar to what are called mutative histologic changes in pancreatic ductal carcinomas. It was difficult to convince the pathologist that the tumor did not actually arise from the pancreas. End to end anastomosis was accomplished in the transverse colon and cecostomy performed. The patient left the hospital in three weeks and has remained well for ten months. The case also shows that, regardless of the size of the tumor exploration and radical removal are indicated. One must be certain before committing oneself to removal of these huge tumors that it is not necessary to injure the portal vein, the superior mesenteric vessels or the hepatic artery. If ligation of any of the large vessels of the mesentery, mesocolon or spleen is necessitated, it is a relatively easy matter to remove segments of the involved intestine or the spleen with the tumor.

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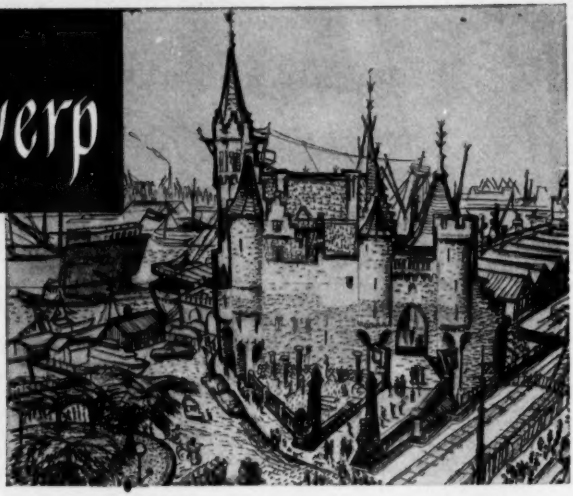

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